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# CHEMISTRY

IN ITS RELATIONS TO

# PHYSIOLOGY AND MEDICINE

BY

GEORGE E. DAY, M.A. CANT. M.D. F.R.S.
Professor of Medicine in the University of St. Andrews

With Five Plates, containing numerous engraved Illustrations

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# INTRODUCTION.

In the present volume I have endeavoured to comprehend in a reasonable space all the most important departments of Physiological Chemistry.

I have taken Lehmann as my principal guide, and have made free use of all his works in this department of chemistry, namely, his "Lehrbuch der physiologischen Chemie," in three volumes, his "Handbuch der physiologischen Chemie" (of which a second edition, much enlarged, appeared last year), and the "Zoochemie," which he published in association with Huppert, in 1858, and which, I believe, is intended to form a section of Gmelin's great work on chemistry. I have likewise borrowed a considerable amount of material from Robin and Verdeil's "Traité de Chimie Anatomique et Physiologique," from Heintz's "Lehrbuch der Zoochemie," from Schlossberger's "Erster Versuch einer allgemeinen und vergleichenden Thier-Chemie," (which, when completed, will form a most valuable addition to chemical literature,) and from Scherer's Annual Reports on the Progress of Physiological Chemistry. In the Chapter on



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"The Urine," I have extracted much important matter from Neubauer and Vogel's comprehensive volume, and the last thirty pages of this chapter are little more than a condensed translation from that work; and in consequence of the extreme importance of the study of the urine and urinary sediments to the physician, I have entered into these subjects at much greater length than their mere physiological importance would warrant. Indeed, I venture to trust that this chapter will be found to contain everything that a medical man requires to know in reference to the subject of which it treats. In the Chapters on "Digestion" and "Respiration," I have made free use of Frerich's celebrated article in Wagner's "Handwörterbuch der Physiologie," and of Vierordt's "Physiologie des Athmens;" while the Chapters on "The Metamorphoses of the Tissues" and "Nutrition," are mainly founded on the works of Bidder and Schmidt, of Bischoff and Voit, and on the corresponding chapters in Lehmann's Handbuch.

The illustrations (with a few exceptions) are taken from Funke's Atlas der physiologischen Chemie.

My aim has been to produce a work equally useful to the senior student and the busy practitioner.

G. E. D.

July 31st, 1860.

# TABLE OF CONTENTS.

## INTRODUCTION.

(1) Physiological Chemistry. — Chemical Relations of Substances. — Physiological Relations. — Chemistry of the Animal Fluids and Solids. — Zoochemical Processes. — Division of the Subject. . . . Pages 1—2.

## BOOK I.

THE ORGANIC SUBSTRATA OF THE ANIMAL BODY; THE PROXIMATE PRINCIPLES ENTERING INTO THE COMPOSITION OF THE SOLIDS AND FLUIDS OF THE ORGANISM.

### CHAPTER I.

THE NON-NITROGENOUS ORGANIC ACIDS.

(2) Different Groups of Non-nitrogenous Organic Acids, with their Formulæ. —Fatty Acids. —Their Formulæ. —Their theoretical Composition. — (3) Oxalic Acid.—Oxalate of Lime.—Its physiological Relations.—Its Origin.— (4) Chemical Characters of and Tests for the volatile Fatty Acids. — (5) Formic Acid.—(6) Acetic Acid.—(7) Metacetonic Acid.—(8) Butyric Acid. — (9) Valerianic Acid. — (10) Caproic, Caprylic, and Capric Acids.—(11) Origin of the above-named Acids.—(12) Their Uses.—(13) Chemical Characters of the solid Fatty Acids.—(14) Margaric and Stearic Acids.—Cocic, Myristic, and Cetic Acids.—Palmitic Acid.—(15) Occurrence of the solid Fatty Acids in the animal Organism.—(16) The Succinic Acid Group.— Succinic Acid.—Sebacic Acid.—(17) The Oleic-Acid Group.—(18) Damaluric and Damolic Acids.—(19) Oleic-Acid.—(20) Doeglingic Acid.—(21) The Benzoic-Acid Group. — Benzoic Acid. — (22) Salicylic Acid. — (23) The Lactic-Acid Group.—Lactic Acid; its theoretical Composition, its Tests, its Occurrence in the animal Body, its Origin, and its Uses. — (24) Non-nitrogenous resinous Acids. — Lithofellic Acid. — (25) Cholic Acid. — Pettinkofer's Test. — (26) Choloidic Acid. — (27) Dyslysin. — (28) Occurrence and Mode of Formation of Cholic Acid. — (29) Tabular View of the Composition of the Non-nitrogenous Acids . . . . . 5—29.

## CHAPTER II.

### NITROGENOUS BASIC BODIES.

(30) Organic Bases. — Volatile Alkaloids. — Trymethylamine. — (31) Non-volatile Alkaloids. — First Group. — Their general Formulæ. — (32) Glycine, Sugar of Gelatin, or Glycocoll. — (33) Sarcosine. — (34) Leucine ; its Appearance under the Microscope ; its chemical Characters ; its Occurrence in the animal Organism ; Lienine and Thymine identical with Leucine. — (35) A Body homologous to Leucine. — (36) Tyrosine ; its microscopical and chemical Characters ; its Occurrence in the animal Organism. — (37) Second Group. —Their general Formulæ. — (38) Creatine ; its Occurrence, and its Functions. — (39) Creatinine. — (40) Urea. — (41) Its chemical Decompositions and Combinations ; its Tests. — (42) Its Occurrence ; its daily Amount ; Influence of Sex, of Food, of Exercise, of Medicines, and of Diseases. — Its Presence in the Blood, Fluids of the Eye, &c.—(43) Its Origin. — (44) Allantoine. — (45) Hypoxanthine. — (46) Xanthine. — (47) Guanine. — (48) Myeline.—(49) Cystine.—(50) Taurine. —(50*) Tabular View of the Composition of the Nitrogenous Bases . . . Pages 30—54.

## CHAPTER III.

### NITROGENOUS CONJUGATED ACIDS.

(51) Mode of grouping of these Acids. — Their theoretical Composition. — (52) Hippuric Acid ; its Tests ; its Occurrence ; its Origin.—(53) Glycocholic Acid (Strecker's Cholic Acid). — (54) Hyocholic Acid. — (55) Taurocholic Acid (the Choleic Acid of Strecker and of Demarçay). — (56) Inosic Acid. — (57) Pneumic or Pulmonic Acid (merely Taurine).—(58) Uric Acid ; its chemical Characters and Decomposition. — (59) Its Combinations : Urate of Soda ; Urate of Potash ; Urate of Ammonia ; Urate of Lime. — (60) Tests for Uric Acid. — (61) Its Occurrence in the animal Body ; Chalkstones. — (62) Its Origin. — (63) Cynuric Acid.— (64) Tabular View of the Composition of the Nitrogenous Conjugated Acids . . . . . 55—70.

## CHAPTER IV.

### HALOID BASES AND SALTS.

(65) Three Groups of Haloid Bases —(66) Oxides of Doegling, Cetyl, Cerotyl, and Melissyl. — (67) Oxide of Lipyl. — (68) Glycerine ; Glycero-phosphoric Acid. — (69) The true Fats or Salts of Oxide of Lipyl. — (70) Human Fat ; Views of Heintz. — (71) Stearin. — (72) Margarin. — (73) Olein. — (74) Occurrence of Fat in the animal Body. — (75) Origin of Fat. — (76) Uses of Fat.—(77) Phenylic (or Carbolic) Acid ; Taurylic Acid.—(78) The Lipoids. — (79) Cholesterin. — (80) Castorin and Ambrein. — (81) Serolin. 71—83

## CHAPTER V.

### THE CARBO-HYDRATES.

(82) The Carbo-hydrates occurring in the Animal Organism; their Formulæ. —(83) Grape-sugar or Glycose; Saccharates.—(84) Trommer's Test for Glycose.—(85) Moore's Test.—(86) Maumène's Test.—(87) The Fermentation-Test. — (88) Occurrence of Sugar (Glycose) in the Animal Organism. — Artificial Diabetes. — (89) Origin of Glycose. — (90) Sugar of Milk; its Occurrence.—(91) Inosite or Muscle-sugar; its Occurrence. — (92) Paramylon; Cellulose. — (93) Tabular View of the Composition of the Neutral Non-nitrogenous Matters . . . . . Pages 84—93.

## CHAPTER VI.

### ANIMAL PIGMENTS OR COLOURING MATTERS.

(94) The Animal Pigments. — (95) Hæmatin; its Functions. — (96) Hæmatoidin. — (97) Bile-pigment (The Cholepyrrhin of Berzelius, the Biliphæin of Simon); its Occurrence, and Origin. — (98) Urine-pigment. — Urohæmatin. — Indigo (see also § 277). — (99) Melanin. — (99 *bis.*) Tabular View of the Composition of the Animal Pigments . . . 94—100.

## CHAPTER VII.

### THE PROTEIN-BODIES.

(100) The Protein-bodies occurring in the Animal Organism. — Protein. — General Characters of the Protein-bodies. — Properties of the soluble Protein-bodies; of the insoluble Protein-bodies. — Millon's test. — (101) Products of the Decomposition of the Protein-bodies. — (102) Albumen; its Formula; its Characteristics; its Tests; its Occurrence; its Origin; its Uses. — (103) Fibrin; its Characteristics; its Composition; its Occurrence; its Origin; its physiological Importance. — (104) Syntonin or Muscle-fibrin. — (105) Casein. — Means of distinguishing it from alkaline Albuminates, or from acid Solutions of Albumen. — Its Occurrence. — Its Origin and Uses. — (106) Globulin or Crystallin. — (107) Hæmatocrystallin. — Tabular View of the ultimate Composition of the Protein-bodies . . . 101—118.

## CHAPTER VIII.

### PROXIMATE DERIVATIVES OF THE PROTEIN-BODIES.

(108) Their general Properties. — (109) Ossein. — Glutin. — (110) Chondrin. — (111) Elasticin. — (112) Fibroin. —(113) Chitin.—(113*) Tabular View of the ultimate Composition of the proximate Derivatives of the Protein-bodies . . . . . 119—124.

## CHAPTER IX.

THE INORGANIC CONSTITUENTS OF THE ANIMAL BODY.

(114) Inorganic Constituents. — Their Division into Three Classes, viz. Substances useful from their Physical Characters ; Substances chemically serviceable ; and Substances incidentally present. — (115) *Substances useful from their Physical Characters.* — (116) Water. — (117) Phosphate of Lime ; its Formula ; its Occurrence ; its Origin and Formation. — (118) Carbonate of Lime ; its Occurrence ; its Solubility in the Animal Fluids. — (119) Phosphate of Magnesia. — (120) Fluoride of Calcium. — (121) Silicic acid. — (122) *Substances Chemically Serviceable.* — (123) Hydrochloric Acid. — (124) Chloride of Sodium. — Its Influence in modifying the Properties of other Substances.—Tabular View of the Quantities of Chloride of Sodium in the Animal Fluids. — (125) Carbonate of Soda. — (126) Phosphates of the Alkalies. — Tabular View of the Quantities in which they occur in the Animal Fluids. — (127) Ammonia and its Salts. — Richardson's Proof of the existence of Ammonia in the Blood. — Its Occurrence elsewhere in the System. — (128) Iron. — (129) *Substances Incidentally present.* — (130) — The Sulphates of the Alkalies. — (131) Carbonate of Magnesia. — (132) Manganese. — Arsenic. — Copper. — Lead. — (133) Sulphocyanogen.

Pages 125—139.

---

# BOOK II.

THE CHEMISTRY OF THE ANIMAL JUICES AND TISSUES.

(134) Classification of the Subject . . . . . 141

## CHAPTER X.

THE DIGESTIVE FLUIDS.

SECTION I. THE SALIVA. — (135) The Saliva ; its physical Characters. — (136) Parotid Saliva. — Ptyalin and its other Constituents. — Submaxillary Saliva — Sublingual Saliva. — (137) Buccal Mucus. — (138) Chemical Composition of ordinary or mixed Saliva. — (139) Incidental and abnormal Constituents ; acid Saliva. — (140) Salivary Concretions. — (141) Daily Quantity of Saliva. — (142) The mechanical Uses of the Saliva. — (143) Its chemical Uses. — (144) The Condition of the Salivary Secretion in Infancy. — (145) Is the Action of the Saliva suspended or continued in the Stomach ?— (146) Saliva exerts no marked chemical Action on any of the Carbo-hydrates except Starch. — (147) Saliva in Rabies . . . . . 144—157.

Section II. The Gastric Juice.—(148) The Gastric Juice.—Mode of obtaining it. — (149) Its physical and chemical Characters, and its Composition. — Its essential Elements. — (150) Its free Acid. — Difference of Opinion on the Subject. — (151) Pepsin. — Peptones. — Schmidt's Pepsin-hydrochloric Acid. — (152) Its mineral Constituents. — (153) Abnormal Constituents. — (154) Daily Quantity of Gastric Juice. — Results yielded by Catherine Kütt. — (155) Its Function. — The Extent of its Solvent Action. — (156) Insufficiency of the Gastric Juice to dissolve the necessary Quantity of Nitrogenous Food. — (157) Why the Stomach itself is not digested . Pages 158—165.

Section III. The Bile. — (158) Its general Properties. — (159) Its essential chemical Constituents: Resinous Acids in Combination with an Alkali, Bile-pigment, and Cholesterin. — (160) Differences between Cystic and Hepatic Bile. — (161) Abnormal Constituents. — Albumen and Urea. — Bilifulvin. — (162) Gall-stones. — (163) Daily Quantity of Bile. — (164) Agents influencing the Amount of Bile. — (165) Functions of the Bile. — (166) Formation of the Bile . . . . . 166—178.

Section IV. Pancreatic Juice. — (167) Its general Properties. — (168) Its chemical Composition. — (169) Its daily Amount. — (170) Its Functions. 178—182.

Section V. Intestinal Juice. — (171) Its physical Properties and chemical Composition. — (172) Its Amount. — (173) Its Functions . . 182—185.

Section VI. The Contents of the Intestinal Canal. — (174) Subjects included in this Section. — (175) The Composition of the semi-solid Contents of the small Intestine. — (176) The Gases contained in the intestinal Canal. — (177) Vomited Matters. — (178) The Contents of the fœtal Intestine and the Meconium. — (179) The Fæces in Health. — Their Odour; their Colour; their daily Quantity; their Composition. — Marcet's Researches. — (180) Yellow Excrement of Infants. — (181) Green Excrements; Causes of the green Colour. — Fat, Blood, &c. in the Fæces. — (182) The Fæces in Disease. — In Typhus; in Cholera. — (183) Intestinal Concretions. 186—200.

## CHAPTER XI.

### THE BLOOD AND ITS ALLIES.

Section I. The Blood. — (184) Physical Characters of the Blood. — (185) Its Coagulation. — (186) Its morphotic Constituents. — Red and colourless Corpuscles or Cells. — (187) The Liquor Sanguinis. — The Clot. — The Serum. — (188) Chemical Composition of the Corpuscles, Liquor Sanguinis, and Blood. — (189) General Arrangement of the Subject. — (190) The Blood-cells; their physical Characters; Variations in their sinking Tendency. (191) Colour of the Blood; due to several conjoined Causes. — (192) Dichromatism of the Venous Blood. — (193) Mode of collecting the Blood-corpuscles on a Filter. — (194) The Cell-membrane of the Red-corpuscles. — Best Method of obtaining it. — (195) Ratio of the Blood-cells to the Plasma.

— Number of Corpuscles in a given Volume of Human Blood. — (196) Chemical Constituents of the Blood-cells. — Hæmatocrystallin ; Hæmatin ; Fats ; Salts ; Preponderance of Potassium-compounds and Phosphates. — (197) The Gases of the Blood. — The State in which they occur in it. — (198) The Colourless Corpuscles. — The Ratio of the White to the Red Corpuscles. — (199) Constituents of the Plasma. — (200) The Coagulation of the Fibrin. — Different Steps of the Process. — (201) Cause of Coagulation. — (202) Circumstances modifying the Period of Coagulation. — (203) Consistence of the Clot. — (204) Form of the Clot. — Buffy Coat. — (205) Quantity of Fibrin in the Blood. — (206) The Serum. — Its occasional Turbidity.—(207) The Quantity of Water in the Serum.—(208) The Quantity of Albumen in the Serum. — (209) Is Casein a Constituent of the Blood-serum ? — (210) Fats. — (211) Extractive Matters. — Various known Substances which formerly passed unrecognised amongst the Extractive Matters. — (212) Mineral Constituents. — (213) Physiological Conditions influencing the Composition of the Blood. — Sex. — Pregnancy. — Age. — Digestion. — Starvation. — (214) Differences between arterial Blood and the Blood of the larger and smaller Veins. — (215) Portal Blood. — (216) Blood of the Hepatic Veins. — (217) Blood of the Splenic Vein. — (218) Menstrual Blood. — (219) Placental Blood. — (220) Influence of Venesection on the Blood. — (221) Blood in different Diseases. — Inflammatory Diseases. — Fevers. — Cholera. — Dysentery. — Bright's Disease. — Plethora. — Anæmia. — Chlorosis. — Typhus. — Puerperal Fever. — Pyæmia. — Leucæmia. — Carcinoma. — Diabetes. — (222) Blood of various kinds of Animals. — (223) Quantity of Blood in the Body. — (224) The Functions and ultimate Disintegration of the Blood-cells . . . . Pages 201—252.

Section II. The Chyle. — (225) The physical Characters of the Chyle. — (226) Its morphotic Elements. — (227) Its chemical Constituents. — (228) Influence of the Food on its Composition. — (229) Quantity of Chyle, 253—256.

Section III. The Lymph. — (230) The physical Characters of the Lymph. — (231) Its morphotic Elements. — (232) Its chemical Constituents and Composition. — (233) Quantity of Lymph . . . . 256—257.

Section IV. Transudations. — (234) Special Characteristics of Transudations, by which they are distinguished from Secretions and Exudations. — (235) Conditions on which Transudation is dependent. — (236) Morphotic Elements of Transudations. — (237) Their Chemical Characters. — (238) — Fibrin. — (239) Albumen. — The Laws on which its Quantity is dependent. (240) Other Constituents. — Casein. — Extractive Matters. — Cholesterin. — Bile-pigment. — Sugar. — Urea. — Creatinine. — Organic Acids. — Salts. — Gases . . . . . 258—266.

## CHAPTER XII.

### THE FLUIDS CONNECTED WITH GENERATION AND DEVELOPMENT.

Section I. The Seminal Fluid. — (241) General Characters of the Seminal Fluid. — Its morphotic Elements. — Effects of various Reagents on the Vitality of the Spermatozoa. — Its chemical Composition . 267—269.

SECTION II. THE FLUIDS OF THE EGG.—(242) The Yelk.—Its morphotic Elements and chemical Composition.—The White.—(243) The Amniotic and Allantoic Fluids in the Chick.—The Amniotic Fluid in the Mammalian Ovum.—The Allantoic Fluid in the Mammalian Ovum.—(244) The (so-called) uterine Milk of the Ruminants. . . . Pages 269—273

SECTION III. THE MILK.—(245) The physical Characters of the Milk.—Colostrum-corpuscles.—Its Reaction.—Its morphotic Elements.—(246) Its chemical Constituents.—(247) Abnormal Constituents.—Albumen; Fibrin; Urea—(248) Passage of Matters into the Milk.—(249) The Colostrum. (250) Various physiological Influences.—Standard of Comparison.—(251) Milk in Diseases.—(252) Milk of Animals.—(253) Daily Quantity of Milk.—(254) Origin of Milk.—Weber's comparative Analysis of the Ashes of Cows' Milk and Ox-blood, showing the Preponderance of Potassium-compounds and Phosphates in the Milk . . 273—285

## CHAPTER XIII.

### THE SECRETIONS OF THE MUCOUS MEMBRANE AND OF THE SKIN.

SECTION I. MUCUS.—(255) Mucus.—Its physical Properties.—(256) Its morphotic Elements.—(257) Its chemical Constituents.—Mucin.—(258) Origin of Mucus . . . . . 286—289

SECTION II. SEBACEOUS MATTERS.—(259) Sebaceous Matters.—Their morphotic Elements.—Their chemical Constituents.—(260) Castoreum.—Secretions of the Cutaneous Glands of certain Reptiles . . 289—291

SECTION III. THE SWEAT.—(261) The Sweat.—Its morphotic Elements and chemical Constituents.—Absence of Lactic Acid, and Presence of Urea in the Sweat.—(262) The Passage of various Substances into the Sweat.—Gases evolved from the Skin.—(263) The Amount of Sweat. 292—295

## CHAPTER XIV.

### THE URINE—INCLUDING URINARY SEDIMENTS AND CALCULI.

(264) The Urine.—Its general Properties.—(265) Acid and alkaline Fermentation.—(266) Its morphotic Elements.—(267) Urea.—Researches of Warncke, Haughton, and Genth, on the Excretion of Urea.—Urea in Typhoid Fever; in Gastric Fever; in Meningitis; in Diabetes.—(268) Uric Acid.—Its daily Quantity.—Does it stand in a definite Ratio to the Urea? Influences of Water, of Quinine, and of certain Diseases in modifying the Quantity of Uric Acid.—Best Method of determining its Amount.—(269) Hippuric Acid.—Investigations of Weissmann and Hallwachs.—Daily Amount of Hippuric Acid.—Absence of Hippuric Acid in Jaundice.—Origin of Hippuric Acid.—Best Method of searching for it in human Urine.—(270) Xanthine.—Its Relation to Hypoxanthine.—(271) Hypoxanthine.—(272)

Allantoine. — (273) Creatinine and Creatine. — Thudichum's Observations on their daily Amount. — (274) Formic, Lactic, and Butyric Acids. — (275) Trymethylamine. — (276) Extractive Matters. — Researches of Scherer and Rummel, in reference to the Amount excreted at different Ages. — Substances included in the term "Extractive Matters." — (277) Urine-pigments. — Schunck's Researches on the Occurrence of Indican (a Substance which yields Indigo Blue) in the Urine. — (278) Mineral Constituents of the Urine. — Chloride of Sodium. — Amount Daily excreted. — Influence of Age, Sex, Fasting, salted and non-salted Food, Exercise, copious Water-drinking, Tea, Coffee, Alcohol, &c., on the Excretion of the Chlorides. — Diminution of the Chlorides in certain Diseases. — Sulphates. — The mean Quantity of Sulphuric Acid excreted daily. — Circumstances modifying the Amount of excreted Sulphates. — Phosphates. — Mean daily Quantity of excreted Phosphoric Acid. — Circumstances modifying its Amount. — Earthy Phosphates. — Iron. — Silica and Fluorine. — (279) Ammonia. — Its Occurrence in the Urine disputed. — (280) Gases. — (281) Water. — Great Variations in its quantity. — Action of Water on the Urinary Secretion. — (282) The free Acid of the Urine. — Method of estimating it. — Influence of Digestion on the Acidity of the Urine. — Researches of Bence Jones and Roberts on this Point. — Influence of Disease on the Acidity. — Connexion between the Acidity of the Urine and the Nature of the Food. — (283) Incidental Constituents. — Modifications which various Substances undergo in their Passage into the Urine. — (284) Rapidity of Elimination. — Circumstances modifying it. — (285) Abnormal Constituents. — Albumen. — The different Conditions which may cause it to appear in the Urine. — Fibrin. — Casein. — Other Protein-bodies. — Fat. — Grape-Sugar. — Inosite, Leucine, and Tyrosine. — Bile-pigment. — Biliary Acids. — Ammonia. — Nitric Acid. — (286) Variations in the Quantity of the Urine. — Influence of Medicines on the Quantity. — Influence of Disease. (287) Variations in the Amount of solid Constituents. — Daily Quantity of Salts. — (288) Influence of various physiological Relations on the Urinary Secretion; of Sex; of Age; of the digestive Process; of different kinds of Food; Researches of Lehmann and of Hammond. — (289) Urine in Disease. — Febrile Urine. — Anæmic Urine. — Difficulties in the Investigation of the Urine in Disease. — (290) Urine of Animals. — (291) Sketch of the Analysis of the Urine. — (292) Tabular View of the daily Urine. — (293) Urinary Sediments. — Importance of their Study. — Urinary Fermentation. — Its Effects on the Formation of Sediments. — Formation of Uric-Acid Sediments. — Formation of Phosphatic Sediments. — Sediments divisible into unorganised and organised. — *Unorganised Sediments;* Uric Acid; the Urates; Conditions under which Sediments of Urates may occur; Causes occasioning these Sediments; Hippuric Acid; Cases in which it occurs as a Sediment; Oxalate of Lime; Importance of this Sediment; earthy Phosphates; Phosphate of Lime; Phosphate of Ammonia and Magnesia; Importance of the Presence of earthy Phosphates as an Evidence of the Alkalinity of Urine; various Causes of an alkaline Reaction of the Urine; Cystine. — *Organised Sediments;* Mucus and Epithelium; Pus; Cancerous and Tubercular Matters; Tubular Casts, occurring (1) as Epithelial Tubes; (2) as Granular Cylinders,

and (3) as Hyaline Cylinders. — Diagnostic Importance of these Casts and Cylinders; Fungi; Infusoria; Spermatozoa.—(294) Tabular *Resumé* of the Sediments. — (295) Urinary Concretions; their Constituents. — *Combustible Calculi*; Uric Acid, Xanthine or Xanthic Oxide, Cystine or Cystic Oxide, Fibrin, Urostealith. — *Incombustible Calculi*; the Urates, Oxalate of Lime, Carbonate of Lime, Fusible Calculi . . . . Pages 296—384.

## CHAPTER XV.

### EXUDATIONS.—PUS.

(296) Characteristics of Exudations. — Difference between Transudation and Exudation. — Cause of their Plasticity. — (297) Different Forms of Exudations.—Fibrinous plastic Exudation.—(298) The Purulent Exudation or Pus. —Pus-Corpuscles.—Cytoid Corpuscles.— Fermentation of Pus.— Relations between the Intercellular Fluids of the Blood and of Pus. — Action of Chemical Reagents on the Pus-Corpuscles.— The Serum of the Pus. — Pyin. —Ordinary chemical Constituents of Pus . . . . . 385—392.

## CHAPTER XVI.

### THE SOLID TISSUES OF THE BODY.

(299.) The Osseous System, composed of organic and inorganic Matters. — Bone-Cartilage or Ossein. — Analysis of different Bones of the Body. — The average Composition of Bone.—Bones at different Ages.—Bones of carnivorous and herbivorous Mammals, of Birds, of Reptiles, and of Fishes. — Morbid Bones. — (300) The Teeth. — Dentine. — Enamel. — Cement. — Carious Teeth.— (301) Cartilage. — True Cartilage and Fibro-Cartilage.— (302) The horny Tissues. — The ultimate Composition of Epidermis, Nails, Horse's Hoof, Hair, and Wool.—The Hair.— Glycogen in the horny Tissues in fœtal Life.—Composition and Properties of Glycogen.—(303) Muscular Tissue.—*Smooth Muscle.*—Its Cell-substance identical with Syntonin.—The Characters of the Fluid permeating smooth Muscle. — *Striped Muscle.* — Substance forming the Fibrils. — Substance of the Nuclei. — The Muscular Juice. — Its Reaction. — Investigation of Du Bois Reymond. — Muscular Contraction dependent on the Presence of Oxygen. — Physical and chemical Characters of the Muscular Juice. — Composition of Muscular Tissue. — Glycogen in fœtal Muscle.—(304) The Brain and Nervous Tissue.— Their morphotic Elements. — Composition of the Brain.—The Brain Fats. — The organic and mineral Constituents of the Brain.—The relative Proportions of Water, Fat, and Phosphorus in different Parts of the Brain. — Action of chemical Reagents on the Nerves. — (305) The Glands and their Juices; their chemical Constituents. — Oidtmann's Researches on their inorganic Constituents . . . . . 393—414

# BOOK III.

## The Zoo-chemical Processes.

### CHAPTER XVII.

#### THE METAMORPHOSES OF THE TISSUES.

(304) The Four essential Factors in the animal Metamorphoses. — (305) *Albumen.* — Its wide Distribution in the animal Body. — Proofs of the primary Origin of all the Tissues (excepting perhaps Fatty Tissue) from Albumen or Casein.—Proofs of the complex Character of the metamorphic Actions going on in the animal Economy. — Importance of the inspired Oxygen. — Gorup-Besanez's Researches on the Action of Ozonised Air on Solutions of Albumen and Casein. — (306) *The Fats.* — Their various uses in relation to Cell-formation.—Changes which the Fat in the Blood undergoes. — Evidence that the Fats are not mere Materials for Combustion. — Does the Organism possess the Power of converting the Protein-Bodies into Fat?—Investigations to determine this Point.—(307) *The Carbo-hydrates.* — Uses of the Sugars and other Carbo-hydrates through their acid Products of Metamorphosis. — Formation of acid Phosphates. — Sugar as a Solvent. — Formation of Fat from Sugar. — (308) *Mineral Constituents.* — Antagonism of acid and alkaline Fluids. — Acid Phosphates and Potash Salts. — Alkalinity of the Blood. — Uses of the Alkalies in the Blood. — Oxidising Action of Alkalies on Sugar, on the Fats and Fatty Acids, on Hæmatin, and on the albuminous Matters of the Blood. — Oxidising Action of the Blood. — Co-existence of an oxidising and a de-oxidising Process. — Chloride of Sodium an active metamorphic Factor. — Observations of Boussingault on the Use of Salt.—Different Modes in which it acts.

Pages 417 – 435

### CHAPTER XVIII.

#### DIGESTION.

(309) Digestion of mineral Substances. — (310) Digestion of the Carbo-hydrates.—Digestion of Grape-Sugar.—Laws of its Absorption.—Behaviour of Cane-Sugar and Sugar of Milk in the intestinal Canal. — (311) Digestion of Starch. — (312) Opinions and Experiments on the Digestion of Gum. — (313) Digestion of Cellulose. — (314) Digestion and Absorption of Fats. — (315) Discussion regarding the Digestion and Absorption of Alcohol. — (316) Protein-Bodies and their Allies; the Changes which they undergo in the intestinal Canal — Peptones. — Parapeptones. — (317) Changes which

Emulsin, Curarine, &c., undergo in the Intestinal Canal. — (318) The various intestinal solvent Fluids. — Discussion regarding the Action of the Pancreatic Juice on the Albuminates. — (319) Absorption of the Peptones. — (320) Daily Amount of intestinal Fluids. — (321) Busch's Observations on a Woman with a Fistula in the Jejunum. — Experiments on the Digestibility of Food . . . . . Pages 436—456.

## CHAPTER XIX.

### RESPIRATION.

(322) Nature of the Respiratory Process. — (323) Ratio of the inspired Oxygen to the exhaled Carbonic Acid. — (324) Volume of the expired Air. — Amount of exhaled aqueous Vapour. — Variations in the inhaled and exhaled Nitrogen. — Volatile Matters in the expired Air. — (325) Percentage of Carbonic Acid in the exhaled Air. — Amount of Oxygen that is retained daily in the System. — (326) Influence of the Rapidity of the Respiration on the Amount of Carbonic Acid. — Influence of the Depth of the Respiration. — (327) Excess of Carbonic Acid in the last Part of an Expiration. — (328) Influence of partial Suspension of the Respiration — (329) Influence of artificial Atmospheres; of Excess of Oxygen; of Excess of Carbonic Acid; of Excess of Nitrogen; of Nitrous Oxide; of Hydrogen; of Carbonic Oxide. — (330) Atmospheric Influences. — Temperature; Moisture; Atmospheric Pressure; Periods of the Day; Periods of the Year. — (331) Internal Conditions of the Organism. — Abstinence. — (332) Influence of the Chemical Nature of the Food. Chemical Explanation of the Results. — Dr. E. Smith's researches on the subject. — (333) Influence of the Quantity of Food. — (334) Influence of Alcohol, Tea, and Coffee. — (335) Influence of Sleep; of Hybernation; of Exercise; of Age; of Sex. — (336) Tabular View of the normal Relations of Carbonic Acid. — (337) Respiration in Animals. — (338) Respiration in Disease. — (339) Origin of the Carbonic Acid. — (340) Animal Heat . . 457—486.

## CHAPTER XX.

### NUTRITION.

(341) Investigations preliminary to that of Nutrition. — (342) Necessity of an Admixture of the different Kinds of Food in certain Proportions. — Investigations of Dr. Hammond on the nutritive Value of Albumen, Starch, and Gum, when taken singly and exclusively. — (342) Digestibility as an Element of the nutritive Value. — (343) Nitrogen as a Measure of the nutrient Value. — Liebig's Table of the Proportions between the Albuminates and the non-nitrogenous nutrient Matters in the most common Articles of Food. — (344). The best relative Admixture of the different Groups of Food. — (345) The necessary Quantity of Food; Method of determining it. — Playfair's Tables. — Vierordt's Calculations. — (346) Quantity of Food

that can be absorbed in a given Time. — (347) Influence of different Kinds of Food on the Composition of the Blood. — (348) Distribution of the final Products of the Food in the Excretions. — (349) Metamorphosis of the Tissues during Inanition. —(350) Effect of the entire Abstraction of Water. — (351) The intestinal Juice as a Measure of the Metamorphosis. —(352) On the Power which certain Substances exert in checking the Metamorphosis of the Tissues. — The physiological Action of Alcohol, of Tobacco, of Tea, and of Coffee . . . . . Pages 487—517.

EXPLANATION OF THE PLATES . . . . . 518—526.

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## CORRECTIONS AND ADDITIONS.

Page 16. Last line. *For* "*Plate I. fig.* 3.," *read* "*Plate I. fig.* 5."

„ 47. Second note. Städeler has repeated Béchamp's experiments, and denies that urea can be formed from albumen by the action of permanganate of potash ; he believes that benzoic acid, which is really formed, was mistaken for urea.

„ 98. Note. *For* "Scherer," *read* "Sicherer."

„ 423. Note. *For* "Hippert," *read* "Huppert."

# PHYSIOLOGICAL CHEMISTRY.

## INTRODUCTION.

(1.) THE object of PHYSIOLOGICAL CHEMISTRY is to elucidate the chemical phenomena attending the vital processes. Physiological Chemistry.

In order to understand these processes, we must have clear conceptions of what may be termed the organic substrata of the animal body; that is to say, we must acquaint ourselves both with the chemical and with the physiological relations of every body or substance occurring in the organism.

The chemical relations of a substance have reference to its general properties, its actual composition (as determined by analysis) and its rational formula, its most important combinations, the products of its metamorphosis, the method of obtaining it in a state of purity, and its tests: while the physiological relations have reference to the fluids or tissues in which it occurs, to the quantity in which it exists, to its origin (whether it be actually produced within the body or introduced from without), and to its uses in the animal economy. In this volume I have entered much more fully into the physiological than into the chemical relations; and I have been led to adopt this course because there are now several excellent manuals*, accessible to every student, in which all the necessary information relating to the purely chemical details is sufficiently given. Chemical relations of substances. Physiological relations.

* Perhaps I may especially indicate Gregory's "Handbook of Organic Chemistry," 4th ed. London, 1856.

Having thus familiarised ourselves with the individual proximate elements of which the body is composed, we next proceed to consider them in reference to their simultaneous occurrence, and to their admixture in the form of animal juices and tissues. The knowledge of the chemical composition of these varying and complex parts of the body is obviously another and a more advanced basis of physiological chemistry, for it is evident that we cannot satisfactorily treat of the great chemico-vital processes without a knowledge of the substances implicated in them; but this investigation is attended with far greater difficulties than the study of the organic substrata, for here we have to deal for the most part with complicated mechanical mixtures whose separation is often an impossibility. The microscope here affords us very useful assistance. It has contributed most materially to our knowledge of those animal fluids which contain morphotic elements (as, for instance, blood, milk, semen, pus, &c.), and of all the solid tissues of the body, as may be seen by a reference to almost every page of the Chapter on Histochemistry. In this division of the volume especial reference has been made to the quantities in which the various glandular products are secreted, a point to which little attention had been paid until the last few years, although the importance of such numerical data, in reference to the general metamorphosis of the tissues, now seems too obvious to require comment.

Chemistry of the animal fluids and solids.

The organic substrata of the animal body, and the constitution and functions of the animal juices and tissues, having been duly considered, we are now prepared to enter upon the highest and most important part of our subject, namely, the study of the great zoo-chemical processes, under which we include the metamorphosis of tissue, digestion, respiration, and nutrition.

Zoo-chemical processes.

Hence the subject-matter of this volume naturally divides itself into three great heads or departments: —

Division of the subject.

1. The organic substrata of the animal body.
2. The chemistry of the animal juices and tissues.
3. The great zoo-chemical processes.

# BOOK I.

THE

## ORGANIC SUBSTRATA OF THE ANIMAL BODY;

OR

THE PROXIMATE PRINCIPLES ENTERING INTO THE COMPOSITION OF THE SOLIDS AND FLUIDS OF THE ORGANISM.

# CHAPTER I.

## THE NON-NITROGENOUS ORGANIC ACIDS.

(2.) In the following sketch of the zoo-chemical elements, we shall adopt the principle of a purely chemical arrangement; that is to say, we shall retain those groups that have been established by the most recent investigations of pure chemistry; but as the physiological importance of a body is always in accordance with its chemical composition, it follows that substances of homologous chemical value must always possess common physiological relations; and that hence our arrangement may at the same time be regarded as a physiological one.

The first great class of substances which we shall describe are the non-nitrogenous organic acids, which may be arranged in the following manner:—

1. Fatty acids with the general formula $C_{2n} H_{2n-1} O_3 . HO$.
2. The succinic-acid group . . . $C_n H_{n-2} O_3 . HO$.
3. The oleic-acid group . . . . $C_{2n} H_{2n-3} O_3 . HO$.
4. The benzoic-acid group . . . $C_n H_{n-9} O_3 . HO$.
5. The lactic-acid group . . . . $C_{2n} H_{2n-1} O_5 . HO$.
6. The non-nitrogenous resinous acids.

We thus commence with bodies of the simplest composition, some of which are probably not actually developed in the living organism; but with which it is necessary that we should be acquainted, as being the derivatives of animal substances. From these groups of comparatively simple bodies we shall gradually pass to those of a more complicated composition — to the nitrogenous basic and neutral bodies, to

nitrogenous conjugated acids, to the haloid bases and lipoids, to the carbo-hydrates, to the animal pigments, and to the histogenetic (or tissue-building) substances — while we shall conclude this portion of the work with a notice of the mineral constituents of the animal body.

## FATTY ACIDS.

$$C_{2n}H_{2n-1}O_3 . HO.$$

Fatty acids.

The first great group to be considered is that of the *Fatty Acids.*

There is a perfect and continuous series of these acids known, from n = 1 to n = 18; but the only ones that at present concern us are: —

| | |
|---|---|
| Formic acid . . . | $= C_2 H O_3 . HO.$ |
| Acetic acid . . . | $= C_4 H_3 O_3 . HO.$ |
| Metacetonic acid . . | $= C_6 H_5 O_3 . HO.$ |
| Butyric acid . . . | $= C_8 H_7 O_3 . HO.$ |
| Valerianic acid . . | $= C_{10} H_9 O_3 . HO.$ |
| Caproic acid . . . | $= C_{12} H_{11} O_3 . HO.$ |
| Caprylic acid. . . | $= C_{16} H_{15} O_3 . HO.$ |
| Capric acid . . . | $= C_{20} H_{19} O_3 . HO.$ |
| Cocic acid . . . | $= C_{26} H_{25} O_3 . HO.$ |
| Myristic acid. . . | $= C_{28} H_{27} O_3 . HO.$ |
| Palmitic acid . . | $= C_{32} H_{31} O_3 . HO.$ |
| Margaric acid . . | $= C_{34} H_{33} O_3 . HO.$ |
| Stearic acid . . . | $= C_{36} H_{35} O_3 . HO.$ |

The acids at the two extremes of the group differ very considerably, both in their physical and chemical characters, and consequently also in their physiological importance, notwithstanding the general analogies that subsist throughout the whole of them: and hence we separate this series somewhat arbitrarily into two groups, the first extending as far downwards as capric acid, and known as the *volatile fatty acids;* while the remaining members are designated the *solid fatty acids.*

There is good reason for believing that the volatile fatty acids are conjugated oxalic acids*; that is to say, that they are acids in which oxalic acid, $C_2O_3 + HO$, is so combined with a carbo-hydrogen, $C_{2n}H_{2n+1}$, as not to affect its own saturating capacity: and on the assumption that oxalic acid constitutes the acidifying principle of the acids of this group, we shall consider it first in the series of acids.

Theoretical composition of the volatile fatty acids.

(3.) *Oxalic acid*† never occurs in the animal organism, except in combination with lime. Oxalate of lime, $CaO.C_2O_3$, occurs in various animal fluids as a white powder, which under the microscope exhibits a distinct crystalline form. When seen with a comparatively low power, these crystals present the appearance of a square envelope; but, when more highly magnified, they may be seen to be octohedrons. (See *Plate I. fig.* 1.) They are insoluble in hot water, in acetic acid, oxalic acid, and in ammonia, but dissolve readily in the stronger mineral acids. Crystals of this salt cannot be confounded with those of chloride of sodium, which often resemble them in form, if we recollect that the latter are very soluble in water. Large crystals of oxalate of lime occasionally present some similarity to crystals of phosphate of ammonia and magnesia, but a careful microscopical examination, and the solubility of the latter salt in acetic acid, will readily decide the question. It is still uncertain whether the *dumb-bell* crystals occasionally found in the urine consist of oxalate of lime, as was originally supposed, as both carbonate of lime and uric acid may assume this form. (See *Plate I. fig.* 2.)

Oxalic acid.

Oxalate of lime.

When oxalate of lime occurs as a constituent of an urinary calculus, its crystalline character is lost, and we cannot apply the microscope to its detection. The following simple test may then be employed. On the application of strong heat to a fragment of the calculus, carbonic oxide is given off, and it becomes converted without charring into carbonate of lime,

* Lehmann's Phys. Chem. (Cavendish Society's Translation), vol. i. p. 39.

† The per-centage composition of this and the other non-nitrogenous acids is given in a table at the end of the chapter.

and ultimately, if the heat be sufficiently prolonged, into quicklime.

Oxalate of lime can be separated from most of the substances with which it is likely to be mixed, by acetic acid or a dilute solution of potash, in neither of which is it soluble.

Oxalate of lime is so frequently found in small quantity in apparently healthy urine, that we can hardly regard it as an abnormal constituent of that fluid. The physiological and pathological relations under which it occurs in augmented quantity will be subsequently described when we treat of the morbid conditions of the urine. It is, moreover, often found in urine which has stood for some time, and in which acid urinary fermentation has taken place, when the perfectly fresh urine presented no trace of it. It has likewise been found in morbid blood; it is often present in the mucus of the gall-bladder, and is scarcely ever absent from the mucous membrane of the impregnated uterus. It is rarely found in the excrements (only after the use of vegetables containing oxalic acid.)

Physiological relations.

The origin of the oxalate of lime found in these cases may be referred to several sources. As the use of vegetable food, especially such as contains oxalates, increases the quantity of oxalate of lime in the urine, we may fairly infer that the oxalic acid is transmitted from the food to the urine. Since, however, the vegetable alkaline salts which abound in plants also increase the oxalate of lime in the urine, we must not refer the augmentation to the former source alone. A well-marked increased excretion of this salt is also observed after the use of drinks rich in carbonic acid, of alkaline bicarbonates, and in short of everything that can overload the blood with carbonic acid; and this is in accordance with another well-established fact, that wherever the respiratory process is affected, or the metamorphosis of the tissues is deranged (an accumulation of carbonic acid in the blood being the result in either case), oxalate of lime may always be found more or less

Its origin.

abundantly in the urine: thus it has been observed in pulmonary emphysema, in the convalescent stage of typhus, &c.

Since the discovery that uric acid can be decomposed by an oxidising agent (peroxide of lead) into urea, allantoine, and oxalic acid, it has been commonly assumed that the oxalic acid of the urine is due to an oxidation of the uric acid, the oxalic acid in this case not being further oxidised into carbonic acid, as usually occurs in the healthy organism; and this view is strongly confirmed by the experiments of Wöhler and Frerichs*, who have shown, by direct experiments, that urates, injected into the veins of dogs, or mixed with the food of men, largely increase both the urea and the oxalate of lime in the urine; and by the observations of Neubauer†, who obtained a similar result when uric acid was introduced into the stomachs of rabbits.

In the great majority of cases the latter is the most probable mode of accounting for the presence of this acid, which we must thus regard as due to the imperfect oxidation of uric acid, and probably of other organic substances in the blood. It must always be regarded as a final product of excretion.

## VOLATILE FATTY ACIDS.

Chemical characters.

(4.) The following are the general characters of these acids. They are liquid, or at all events fusible, at a temperature not exceeding 86°, and do not solidify and crystallise till it is reduced below the freezing point. They are so volatile that at an ordinary temperature their vapour is extremely irritating to the eyes and nostrils. They can be distilled without decomposition, and boil at a temperature which stands in a definite ratio to the number of atoms of carbo-hydrogen, the boiling point rising by rather more than 34° for every two atoms of CH. They are soluble in water, alcohol, and ether, but their solubility in water diminishes as their amount of carbon in-

* Ann. d. Ch. u. Pharm. 1848, vol. lxv. p. 340.

† Ibid. 1856, vol. xcix. p. 206.

creases. They redden litmus powerfully, and unite with bases to form salts, most of which are soluble in water and crystallisable; as, however, in the case of the acids, the solubility decreases as the carbon increases, and hence the salts of capric acid are the least soluble.

The first two acids of this group, formic and acetic acid, are the most powerful; strictly speaking they have no right to be called oily or fatty. As the number of atoms of CH increases, the acids become by degrees less energetic, but assume the character of oils, and finally of fats. Metacetonic acid is only slightly oily; capric acid is a solid fat.

Tests for the volatile fatty acids.

As there are great difficulties in determining quantitatively, and in some cases even qualitatively, the presence of these volatile fatty acids, we shall merely notice such tests and reagents as can without much danger of fallacy be applied by a student ordinarily versed in chemistry.

To detect these acids in an animal fluid we must first isolate them. The following are the general steps of the process to be adopted. We place the fluid in a retort, add a few drops of strong sulphuric acid to liberate them from the bases with which they are combined, and distil. The distillate, which is usually only faintly acid and somewhat opalescent, is saturated with carbonate of soda, evaporated on a water-bath, and redistilled with a little dilute sulphuric acid, without the application of heat. If several acids of this group are simultaneously present, they may be separated by fractional distillation; formic acid, from its boiling point being the lowest, comes over first, and the others in succession according to their boiling points.

*a.* Formic acid may be distinguished from the other acids of this group, by its power of reducing the oxides of silver and mercury.

*b.* Acetic acid resembles formic acid, and in this respect, also, meconic and hydrosulphocyanic acids, in producing an intense red colour with perchloride of iron; but it may at

once be distinguished from formic acid, by its not having the power of reducing the oxides of silver or mercury. If there should be any possibility of the presence of either of the two other acids, it may readily be distinguished from meconic acid by the solubility of the acetate of lime (the meconate of lime being insoluble in water), and from hydrosulphocyanic acid by the circumstance that the red solution of sulphocyanide of iron, if boiled with a little ferrocyanide of potassium, very soon precipitates Prussian blue, which is not the case with the acetate of the peroxide of iron.

*c.* The odour of several of these acids (*e. g.* acetic, valerianic, and butyric acids) is sufficiently characteristic to be ranked amongst the tests.

*d.* The presence of metacetonic acid can only be ascertained with certainty by the elementary analysis of one of its salts, or by the determination of the atomic weight or saturating capacity; and the same observation equally applies to the other acids of this group.

Formic acid.

(5.) As its name indicates, ***Formic acid*** occurs in ants (especially ***Formica rufa***); Will has recently shown that the active poisonous principle in certain caterpillars is formic acid, and it is highly probable that the irritation caused by the stings of various insects is due to this acid; Scherer has found it in association with other acids of this group, in the muscular and splenic juices, and in leucæmic blood; Campbell has found it in the blood, urine, and vomited matters; and Schottin has proved that it is by far the chief of the volatile constituents of the sweat; and Gorup-Besanez has found it in considerable quantity in the thymus gland.

Acetic acid.

(6.) ***Acetic acid*** was found by Scherer, in association with formic acid, in the muscular and splenic juices, and in leucæmic blood, and by Gorup-Besanez in the juice of the thymus gland; Lehmann and others have found it in the gastric juice in cases of impaired digestion; and Schottin has proved that it is a constant ingredient both of normal and morbid sweat.

Meta-cetonic acid.

(7.) As *Metacetonic acid* is readily formed in the laboratory during the oxidation both of the fats and of the albuminous bodies, there is no apparent reason why it should not occur in the animal organism. Schottin thinks that he has found it in sweat.

Butyric acid.

(8.) *Butyric acid* has been found by Scherer in the muscular and splenic juices, and by Lehmann in the juice of the muscular coat of the stomach. Salts of this acid have not yet been discovered in the blood, although they probably exist there. It occurs in a free state in the sweat, although in less quantity than formic or acetic acid. The milk contains, in addition to other fats, as margarin and olein, one which on saponification yields butyric acid, together with caproic, caprylic, and capric acids. This acid has been found in the human gastric fluid by Gruenewaldt, but Frerichs had previously observed that after the use of amylaceous food there is often a strong odour of butyric acid in the contents of the lower part of the ileum and of the colon; Ragsky and Percy have, moreover, discovered it in the fæces.

Valerianic acid.

(9.) *Valerianic acid* in association with leucine has been found in the urine in typhus fever by Frerichs; this leucine had probably undergone a partial decomposition into valerianate of ammonia. See § 31.

Caproic, caprylic, and capric acids.

(10.) As *Caproic, Caprylic,* and *Capric acids,* in combination with glycerine or oxide of lipyl, exist in the milk, it is most probable that they also occur in the blood. From the peculiar odour of the sweat it is very likely that one or more of these acids are present in minute quantity in it.

Their origin.

(11.) As most of the above named acids have been artificially obtained in the laboratory by the oxidation of the fats and albuminous bodies, and as the most essential processes in the living organism are based on a process of oxidation, the presence of the volatile fatty acids in the animal fluids is thus readily accounted for. From Schottin's observations on the sweat, their formation seems to be increased, as

is also the case with oxalic acid, when the respiratory process, and, consequently, the general oxidation of the system, is impeded. In some cases, however, the acid may be directly introduced from without; thus, it is by no means certain that the ants actually produce formic acid, for we know that it is contained in juniper and other berries, and in fir-cones, which are much sought after by these insects: and in other cases, especially in that of butyric acid, it is extremely probable that the fatty acid is formed in the lower portion of the intestinal canal from carbo-hydrates taken as food, all the necessary conditions for the development of this kind of fermentation being usually present there.

Heintz* has made an experiment which seems to prove that the acids found by Scherer in the muscular juice do not pre-exist there, but must have been mere products of the decomposition of the flesh that ensued during his operations. He failed in obtaining any trace of a volatile fatty acid from 50 pounds of horse-flesh.

(12.) From the preceding remarks on the occurrence of these acids, we are justified in believing that they play no very important part in the animal economy. When occurring in the stomach and intestinal canal, they must be regarded as mere incidental substances due to the temporary establishment of a special fermentative process; and their presence in the two great depurating fluids, the sweat and the urine, clearly indicates that they are true products of excretion. They must therefore be classed amongst the products of the regressive metamorphosis of tissue; that is to say, they originate from those changes which the tissues and juices undergo in the discharge of their physiological functions. In the perfectly healthy state they, for the most part, undergo further oxidation, and are finally excreted in the form of carbonic acid and water; but when, from the establishment of

Their uses.

* Lehrbuch der Zoochemie, Berlin, 1853, p. 447.

any morbid process, the normal oxidation of the blood is impeded, these substances are found in increased quantity in the excretions.

### SOLID FATTY ACIDS.

Chemical characters.

(13.) These acids are distinguished from those which have just been considered by the following properties:—At an ordinary temperature they are solid, white, and crystalline, are devoid of odour or taste, make a persistent greasy spot on paper, and for the most part cannot be submitted to ordinary distillation without decomposition. They are perfectly insoluble in water, dissolve in boiling alcohol, from which they separate in a crystalline form on cooling, and are readily soluble in ether. Their alcoholic solutions only faintly redden litmus. They unite with most bases, and form insoluble salts, their alkaline salts — the soaps — being alone soluble in water.

Margaric and stearic acids.

(14.) The following properties of *Margaric* and *Stearic acids*, the most important bodies of this class, may assist in their identification. Margaric acid separates from a hot alcoholic solution in glistening groups of very delicate needles, which under the microscope appear in variously sized grass-like bunches of ensiform or lily-leaf-shaped crystals, or in star-like forms (*Plate I., fig.* 3.); while stearic acid crystallises in white glistening needles or leaflets, which when magnified appear as very elongated lozenge-shaped laminæ, with the obtuse angles rounded off, as in the whetstone-like crystals of uric acid (*Plate I., fig.* 4.); these crystals are, however, much longer, and have a far shorter transverse diameter than the corresponding crystals of uric acid; they often collect at one spot, and present the appearance of whorl-shaped clusters, the acute angles slightly overlapping one another.

Their fusing points are 133° and 167° respectively. As the two acids are commonly associated together, Gottlieb has

determined the fusing points of their mixtures in various proportions. His table is given in Lehmann's "Physiological Chemistry," vol. i. p. 111., and may serve to assist in an approximate determination of the ratios in which they occur.

Heintz, in one of his latest memoirs * on the fats and fatty acids, denies the existence of margaric acid, and maintains that it is a mixture of about ten parts of palmitic acid with one part of stearic acid. This view is, however, not generally adopted.

Other solid fatty acids.

The recent researches of Heintz show that the following acids of this sub-group occur in the animal economy.

*Cocic, Myristic,* and *Cetic acids* have been detected by him†, in spermaceti, in combination with ethal (or hydrated oxide of cetyl). See § 66.

*Palmitic acid* has been found by the same chemist‡ (but by no one else) in human fat, in mutton suet, and in spermaceti.

Their occurrence.

(15.) Margaric acid occurs either in a free state or in combination with alkalies, in most of the animal fluids, with the exception of the urine; being free in acid fluids, and in a state of combination in those with an alkaline reaction. It is always accompanied by oleic acid or oleates. Free margaric acid is chiefly found in acid pus, in the fluid of ovarian dropsy, and in the excrements after the use of vegetable food or of purgative medicines; while alkaline margarates occur in the blood, chyle, saliva, exudations, and most abundantly in the bile and in ordinary pus.

In combination with oxide of lipyl (see § 72.) this acid forms margarin, the most widely diffused of all the anima fats.

Stearic acid never occurs free or in combination with the alkalies, unless in association with margaric acid. Like margaric acid, it unites with oxide of lipyl to form stearin, which almost always accompanies margarin.

* Pogg. Annal. vol. lxxxvii. p. 553; or Lehrb. d. Zoochem. p. 1074.
† Lehrb. d. Zoochem. p. 489. ‡ Ibid. p. 428.

We shall postpone our observations on the origin and importance of these acids, till we treat of the fats in which they mainly occur. (See §§ 75 and 76.)

### THE SUCCINIC-ACID GROUP.

$$C_nH_{n-2}O_3 . HO.$$

(16.) Only one of the acids of this group, namely succinic acid, has as yet ever been detected in the animal organism; the other acids, namely, lipic, adipic, pimelic, suberic, and sebacic acids, are only of interest in zoo-chemistry, in so far as, like many of the acids of the preceding group, they are products of decomposition of many animal substances, and especially of the fats. They are probably, like the last group, conjugated oxalic acids.

Succinic acid.

*Succinic acid* is represented by the formula $C_4H_2O_3.HO$, or, according to the above hypothesis, by $(C_2H_2)\ C_2O_3.HO$. It is of such rare occurrence that it is unnecessary to enter into any chemical details regarding it. It was once found by Heintz* in the fluid contents of hydatids in the liver, where it has been re-discovered by Bödeker†; and it has recently been detected by Gorup-Besanez‡, in the thymus gland of calves and in the spleen and thyroid gland of oxen, and, by W. Müller§, in the fluid of hydrocele.

Sebacic acid.

*Sebacic acid*, which is represented by the formula $C_{10}H_8O_3.HO$, or as a conjugated acid by $(C_8H_8)\ C_2O_3.HO$, is deserving of notice, as being only formed during the dry distillation of oleic acid. Hence we may determine the presence and amount of olein in a fat, from the presence and amount of the sebacic acid. It crystallises in whorled clusters, similar to margaric acid, or in laminæ radiating from a centre. (See *Plate I. fig.* 3.)

* Op. cit. p. 228.

† Zeitsch. f. rat. Med. 1855, vol. vii. p. 137.

‡ Ann. d. Ch. u. Pharm. 1856, vol. xcviii. p. 40.

§ Zeitsch. f. rat. Med. 1856, vol. viii. p. 130.

## THE OLEIC-ACID GROUP.

$$C_{2n}H_{2n-3}O_3.HO.$$

(17.) The acids of this group requiring notice, are

| | |
|---|---|
| Damaluric acid . . . | $C_{14}H_{11}O_3.HO.$ |
| Damolic acid . . . | $C_{26}H_{23}O_3.HO.$ |
| Oleic acid . . . . | $C_{36}H_{33}O_3.HO.$ |
| and Doeglingic acid . . . | $C_{38}H_{35}O_3.HO.$ |

The first two of these are oily volatile fluids which are slightly soluble in water, but dissolve freely in alcohol and ether, and redden litmus; they may be regarded as standing to the two other acids in much the same relation as the volatile to the solid fatty acids.

The last two exist at an ordinary temperature as oily fluids, and in most of their physical, and in many of their chemical properties, resemble the solid fatty acids.

Damaluric and Damolic acids.

(18.) *Damaluric* and *Damolic acids* were discovered by Städeler amongst the products of distillation of the urine of the cow, and of man. As they have not as yet been discovered in any other fluid, and occur in very minute quantity, they present little physiological interest.

Oleic acid.

(19.) *Oleic acid*, when perfectly pure, and at a temperature above 57°, is a limpid oily fluid, devoid of taste and smell, and exerting no action on litmus; at 39° it solidifies into a hard, white, crystalline mass. When heated it becomes decomposed, and yields on dry distillation not only carbon, carbonic acid, and carbo-hydrogens, but capric and caprylic acids, and sebacic acid. It possesses the distinctive character of being the only substance which on dry distillation yields the last-named acid, which we may readily distinguish from the simultaneously formed capric and caprylic acids, by the shape and arrangement of its crystals.

Its occurrence.

Oleic acid is invariably found wherever margaric and stearic acids occur; in the blood and in the bile it is com-

bined with alkalies; it is found free in acid pus; and it is combined with oxide of lipyl, forming olein, in the subcutaneous adipose tissue, and indeed wherever free fat occurs in the animal body.

The uses and origin of this acid will be noticed when we reat of the animal fats generally.

Doeglingic acid.

(20.) *Doeglingic acid* is of no special interest; it was found by Scharling, in the oil of the Doegling (the *Balæna rostrata* of the older zoologists, but now regarded as a species of Hyperoödon).

### THE BENZOIC-ACID GROUP.

$$C_nH_{n-9}O_3.HO.$$

(21.) We should not refer to this group of acids, if it were not that its representative, benzoic acid, sometimes occurs in the animal fluids, and that the change which it undergoes in the animal body elucidates certain points connected with the metamorphosis of tissue.

Benzoic acid.

*Benzoic acid* is represented by the formula $C_{14}H_5O_3.HO$; or, if it be regarded as a conjugated oxalic acid, by $(C_{12}H_5)C_2O_3.HO$. It is solid at ordinary temperatures, but fuses at about 250°, and boils and sublimes without decomposition at 462°. When obtained in this way, it occurs in delicate needles; when precipitated from a spirituous solution, it usually crystallises in scales. It is slightly soluble in cold water, dissolves freely in hot water, is soluble in alcohol and (to a less extent) in ether, and its solutions redden litmus.

The only acid occurring in the animal body with which it is likely to be confounded is hippuric acid. The mode of distinguishing these acids is given in § 52.

It is only in the urine that the presence of benzoic acid has ever been suspected; and here it merely occurs as a product of the decomposition of hippuric acid, which, as will be presently shown, may be regarded as a conjugated benzoic acid.

(See § 52.) It is never found in the fresh urine even of the herbivora, although Liebig at one time held the opposite opinion. After the use of benzoic acid we always find a large quantity of hippuric acid in the urine*; it reappears, however, unchanged in the sweat.

(22.) *Salicylic acid* is an analogous acid, differing only from benzoic acid in containing two more atoms of oxygen. It occurs in the urine, in association with salicylous acid, after the use of salicin; as these acids occur in castoreum, in consequence of the willow-bark being a favourite article of food with the beaver, they may be regarded as normal constituents of the urine of that animal. Salicylic acid.

### THE LACTIC-ACID GROUP.

$$C_{2n}H_{2n-1}O_5 . HO.$$

(23.) The three following acids belong to this group:—

| | |
|---|---|
| Glycic acid . . . . | $C_4 H_3 O_5 . HO.$ |
| Lactic acid . . . . | $C_6 H_5 O_5 . HO.$ |
| and Leucic acid . . . . | $C_{12}H_{11}O_5 . HO.$ |

As neither glycic nor leucic acid has been as yet detected preformed in the animal organism, we shall confine our remarks to *Lactic acid.*

The researches of Strecker seem to have established the fact that lactic acid should be regarded as formic acid conjugated with aldehyde† as an adjunct; its rational formula therefore is $C_4H_4O_2.C_2HO_3.HO$. Lactic acid.

* Duchek has made some important observations regarding the proportions in which hippuric acid occurs in the urine after the ingestion of benzoic acid. When 1 gramme of benzoic acid was taken, 0·714 of a gramme of hippuric acid was excreted; 2 grammes were followed by the excretion of 1·857 grammes of hippuric acid and 0·421 of a gramme of benzoic acid; and 4 grammes, by 1·714 of hippuric acid and 2·500 of benzoic acid. Hence the limit at which the conversion ceases is soon reached.

† The formula for aldehyde is $C_4H_3O . HO$. It is a clear colourless liquid

Lactic acid, when deprived as much as possible of water, is an oily fluid which does not solidify at the greatest cold, with a strongly acid taste, no odour, and soluble in water, alcohol, and ether, in all proportions; it has a very acid reaction, decomposes when heated, and displaces not only the volatile acids, but some of the stronger mineral acids from their salts.

The determination of the presence of lactic acid is one of the most difficult tasks in analytical chemistry, and we have generally to found our decision regarding its occurrence on the crystalline form of its salts. The most characteristic forms are those of the lactates of lime, copper, and zinc. The best method of detecting small quantities of lactic acid in animal matters is that of Scherer, of which I have given an abstract in the appendix to the third volume of Lehmann's "Physiological Chemistry."

Its occurrence.

Lactic acid, both in its free and combined state, occurs very frequently, but by no means invariably, in the gastric juice, in association with hydrochloric acid, which is usually present in that fluid. In the saliva it has only been detected with certainty in cases of diabetes. The acid reaction which the contents of the duodenum and jejunum present, especially after the use of vegetable food, mainly depends on lactic acid, and crystals of lactate of lime (*Plate I. fig.* 6.) have been repeatedly obtained by Lehmann from an alcoholic solution of the contents of the duodenum of the horse. The strong acid reaction presented by the contents of the large intestine after the ingestion of amylaceous and saccharine food, is due to the production, by fermentation, of this acid, which is then accompanied by butyric acid.

It has not yet been ascertained whether lactates are constantly present in the chyle. Lehmann detected them in the chyle obtained from the thoracic duct in two horses, one of

of a peculiar ethereal odour. It is called aldehyde, because it may be regarded as alcohol deprived of part of its hydrogen,— *al*-cohol *de-hyd*-rogenatum.

which had been fed two hours before its death with oats, and the other with starch-balls. Hence it may be regarded as an established fact that, even if not always present, they certainly occur in this fluid during the digestion of amylaceous food.

No one has definitely established the presence of lactates in the lymph; but as we cannot conceive that the lactic acid, which is so abundantly formed in the muscles, can be carried off by any other channel than by the lymphatics, and as, further, lymph, whose reaction was scarcely or not at all alkaline, and whose albuminous constituents were removed previous to incineration, has been then found to yield much carbonated alkali, they most probably exist in this fluid.

The recognition of lactates in the healthy blood, into which they must be transmitted from the intestinal canal and the muscular tissue, is impossible in consequence of their very rapid oxidation and perfect combustion. The rapidity with which lactates in the blood are converted into carbonates is proved by experiments made by Lehmann and others, of injecting lactate of soda into the jugular veins of dogs; after five, or at latest after twelve minutes, the urine exhibited an alkaline reaction, which showed that the lactate had been oxidised and converted into a carbonate. Lactic acid may, however, collect abnormally in the blood, in cases in which the normal oxidation of that fluid is impeded, in such quantities as to be detected chemically. Blood, with an acid reaction due to the presence of this acid, has been observed by Scherer and Lehmann in puerperal fever, pyæmia, and leucæmia.

Lactic acid has been found, both in a free and in a combined state, in purulent exudations, especially in cases of puerperal fever.

Although this acid was originally obtained by Scheele from milk, it does not occur in the normal human milk, which generally has an alkaline reaction. It is only in an abnormal state, or after a purely animal diet, that milk with an acid

reaction, due probably to lactic acid, is secreted. Healthy milk, however, soon acquires an acid reaction, which is dependent on the formation of lactic acid from its sugar by fermentation. Schlossberger has shown that in the carnivora this fluid is usually acid, the reaction being doubtless due to lactic acid.

Free lactic acid exists in such abundant quantity in the muscles of carnivorous as well as of herbivorous animals, that Liebig believes that it is more than sufficient to saturate the alkali of the alkaline fluids of the animal body. It likewise occurs in the juice of the smooth muscles and of the spleen.

Gorup-Besanez found it in small quantity in the thymus gland of the calf, and in the spleen, liver, pancreas, kidneys, lungs, and thyroid gland of the ox; and von Bibra has found it in the brain.

The recent investigations of Schottin, made under the immediate superintendence of Lehmann, disprove the existence of this acid in normal and even in morbid sweat, although several of the older chemists, and recently Favre, maintain that it occurs in that fluid.

Lactic acid is sometimes, but not always, found in the urine. "In all cases," says Lehmann, "where the supply of lactates to the blood is very great — whether this depends on an excess of acid being formed in the muscles, or on the use of a diet tending to produce it, or on an imperfect process of oxidation in the blood — lactic acid may be detected in the urine with all the certainty which in the present state of chemistry can be expected. Hence it is that in the urine of the same individual lactic acid may on one day be present and on another absent; — why in many persons no lactic acid can be detected in the urine, and in others again (in whom the respiratory process is imperfectly accomplished) it is constantly present in the urine; — why stall-fed animals, living on amylaceous fodder, excrete lactic acid by the kidneys (and in part also by the mammary glands), whilst under other con-

ditions this acid cannot be discovered in their urine; — and why, finally, in most febrile diseases lactic acid may be recognised in the urine." Thus lactic acid occurs in the urine under the same conditions which give rise to the development of oxalic acid (see § 3); and hence the detection of oxalate of lime by the microscope leads us to the inference that lactic acid is probably also present. It has been found in considerable excess in the urine in cases of rachitis and osteomalacia. In examining this secretion for lactic acid, we must not overlook the fact that it is formed by a process of fermentation, probably from that unknown matter to which we apply the term *extractive*, when urine is exposed to the action of the atmosphere.

Lassaigne believes that he has found lactate of soda in the allantoic fluid of a calf.

Schmidt has separated lactic acid from the strongly acid fluid yielded by the softened cylindrical bones in a case of osteo-malacia.

Its origin.

The lactic acid, which is thus widely diffused throughout the animal fluids, may be referred to a treble origin. No one can doubt that the acid found in the contents of the intestines, and in the chyle after the digestion of vegetables, owes its formation to the amylaceous or saccharine matters contained in the food undergoing a change similar to that which takes place in the fermentation of milk; moreover, the sugar which is formed in the liver, both in carnivorous and herbivorous animals, is similarly converted in the blood into lactic acid; while the acid which is found in such large quantity in the muscles cannot be referred to these sources, but must be considered as a product of the metamorphosis of the muscular fibre — a view confirmed by the fact that the amount of free acid is proportional to the extent to which the muscles had been previously exercised.

Its uses.

The physiological value of lactic acid is by no means inconsiderable; for, in the first place, in association with free

hydrochloric acid, it essentially contributes to the digestive power of the gastric juice, no other mineral or organic acid possessing the property of being able to replace these; secondly, the free lactic acid in the intestinal canal assists materially in promoting an absorption or transudation of the digested food into the alkaline blood or lymph, in accordance with the known laws of endosmosis*; thirdly, the alkaline lactates are excellent supporters of animal heat, in consequence of the rapid combustion which they undergo in the blood; and, lastly, it is probable (as Liebig supposes) that an electric tension, influencing the function of the muscles, is established by the acid muscular juice and the alkaline contents of the capillaries.

### NON-NITROGENOUS RESINOUS ACIDS.

(24.) There are two acids† belonging to this group which require to be noticed in this place, namely —

Lithofellic acid . . . $C_{40}H_{36}O_7 . HO$,
and Cholic acid . . . . $C_{48}H_{39}O_9 . HO$.

Lithofellic acid.

*Lithofellic acid* is a crystalline resinous acid which exists only in certain bezoars which are obtained from the intestines of various species of goats inhabiting the East. Whether it is derived from the food of those animals, or whether it takes its origin in the bile, is as yet undecided.

Cholic acid.

(25.) *Cholic acid*‡ occurs in colourless glistening crystals,

* See especially Graham's Bakerian Lecture on Osmotic Force, in the "Philosophical Transactions," for 1854, p. 227.

† To these we ought, perhaps, to add benzoglycic acid, $C_{18}H_7O_7 . HO$, although it has never yet been found preformed in the animal organism. It receives its name because it may be regarded as a conjugated compound, composed of benzoic and glycic acids, $C_{14}H_5O_3 . C_4H_3O_5$, being readily decomposed into these two acids when warmed with a dilute acid. It is of interest, as indicating the probable theoretical composition of hippuric acid. (See § 51.)

‡ This is Demarçay's *cholic acid*; it is the *cholalic acid* of Strecker. The names of the biliary acids are very confusing, the same term being frequently applied by different chemists to very different substances.

which effloresce on exposure to the air, and have a peculiarly bitter taste. It is only slightly soluble in water, but dissolves very readily in alcohol, especially when heated, from which it crystallises in tetrahedra; it dissolves rather less freely in ether, from which it separates in rhombic tablets. (*Plate I. fig.* 7.) This acid strongly reddens litmus, fuses at 383°: at a slightly higher temperature it loses its atom of basic water, and is converted into choloidic acid, and at 554° into dyslysin. If boiled for some time in hydrochloric acid, it ceases to be crystallisable and is converted into choloidic acid, and on further boiling, it loses its acid properties and forms dyslysin. By the action of boiling nitric acid, it is for the most part converted into capric, caprylic, and cholesteric acids. It dissolves in sulphuric acid, and, if we add a drop of syrup to the solution, it assumes a beautiful purple tint. This, which is known as Pettenkofer's test, is equally applicable whether the cholic acid be free, or combined with the adjuncts with which it is naturally conjugated in the bile, or metamorphosed into choloidic acid: hence we can apply it to discover generally either the presence of this essential biliary acid, or of one of its derivatives. The following is the best method of proceeding in testing for biliary matter in a fluid which is suspected to contain it. The alcoholic extract of the fluid must be dissolved in a little water, with which we must then mix a drop of syrup (consisting of 1 part of sugar to 4 of water), and strong sulphuric acid must be added by drops to the mixture. The fluid first becomes turbid, from the separation of the cholic acid, which, however, dissolves on the addition of a little more sulphuric acid: for a few moments its colour is yellowish; it soon, however, becomes of a pale cherry colour, then of a deep carmine, of a purple, and, finally, of an intense violet tint. We must not allow the temperature to be raised by the sulphuric acid beyond about 120°, which seems to be the most favourable heat for the development of the reaction. Should the fluid at first assume only a cherry-red or a deep

Pettenkofer's test.

carmine tint, it must be allowed to stand for some time. Any kind of sugar may be employed, or acetic acid may be used in its place.

It has been recently discovered that oleic acid and certain ethereal oils possess a similar power of developing a violet tint with concentrated sulphuric acid and sugar; as, however, the reaction takes place very slowly in these fluids, and merely on the surface (it being due to the absorption of oxygen), the value of the test is not affected.

As choloidic acid and dyslysin are sometimes found in the animal body in association with cholic acid, it is expedient briefly to notice their composition and leading characters.

Choloidic acid.

(26.) *Choloidic acid*, as it exists in its salts, is perfectly isomeric with cholic acid. We have already mentioned its formation from cholic acid by the aid of heat and of hydrochloric acid; it seems likewise to be occasionally produced, in association with dyslysin, from the decomposition of the bile in the lower part of the small intestine (see § 175). In a state of purity it is a white, amorphous, resinous, pulverisable mass, which is insoluble in water, but dissolves readily in alcohol; it is almost insoluble in ether, which thus serves to distinguish it from cholic acid.

Dyslysin.

(27.) *Dyslysin* seems to be formed from choloidic acid by the abstraction of 3 atoms of water, its composition being represented by the formula $C_{48}H_{36}O_6$. Its mode of production has been already mentioned. It forms a grayish white mass, which is soluble in ether, but insoluble in water, cold alcohol, acids, and alkalies; hence its name. When boiled with an alcoholic solution of potash it is reconverted into choloidic acid.

Occurrence of cholic acid.

(28.) In the normal bile cholic acid is always found in conjugation with taurine or glycine (see §§ 53 and 55), and in this state of combination it sometimes passes, in abnormal conditions of the system, into the blood and other fluids. In the intestinal canal, on the other hand, it is very soon separated from its nitrogenous adjuncts, and is partly con-

verted into choloidic acid and dyslysin. It is found in very small quantity in the normal excrements, but to a considerably larger amount in cases of diarrhœa.

Its formation.

Cholic acid is unquestionably formed in the liver, but we do not definitely know from what materials it is produced in that organ. Lehmann inclines to the view that, since fats contribute essentially to the formation of bile (as is shown both by accurate comparative analyses of the blood entering and leaving the liver, and by careful statistical observations on living animals), it is very probable that this acid consists of a combination of oleic acid and a carbo-hydrate $C_{12}H_6O_6$; and this view is further supported by the fact that we know that one carbo-hydrate, sugar, is formed in considerable quantity in the liver. Moreover, a comparison of the respective products of oxidation of cholic and oleic acids strengthens the hypothesis; for, when treated with concentrated nitric acid, cholic acid yields precisely the same products of decomposition as oleic acid, and additionally a carbo-hydrate, namely, cholesteric acid, whose composition is represented by the formula $C_8H_4O_4$.

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(29.) TABULAR VIEW OF THE COMPOSITION OF THE NON-NITROGENOUS ACIDS.

| *Oxalic acid*, $C_2O_3 . HO$. | | *Formic acid*, $C_2HO_3 . HO$. | |
|---|---|---|---|
| Carbon | 26·667 | Carbon | 26·087 |
| Oxygen | 53·337 | Hydrogen | 2·174 |
| Water | 20·000 | Oxygen | 52·174 |
| | | Water | 19·565 |

| *Acetic acid*, $C_4H_3O_3 . HO$. | | *Metacetonic acid*, $C_6H_5O_3 . HO$. | |
|---|---|---|---|
| Carbon | 40·000 | Carbon | 48·649 |
| Hydrogen | 5·000 | Hydrogen | 6·757 |
| Oxygen | 40·000 | Oxygen | 32·432 |
| Water | 15·000 | Water | 12·162 |

| *Butyric acid,* $C_8H_7O_3 . HO.$ | |
|---|---|
| Carbon . . | 54·545 |
| Hydrogen . . | 7·955 |
| Oxygen . . | 27·273 |
| Water . . . | 10·227 |

| *Valerianic acid,* $C_{10}H_9O_3 . HO$ | |
|---|---|
| Carbon . . | 58·824 |
| Hydrogen . . | 8·823 |
| Oxygen . . | 23·530 |
| Water . . . | 8·823 |

| *Caproic acid,* $C_{12}H_{11}O_3 . HO.$ | |
|---|---|
| Carbon . . | 62·069 |
| Hydrogen . . | 9·483 |
| Oxygen . . | 20·689 |
| Water . . . | 7·759 |

| *Caprylic acid,* $C_{16}H_{15}O_3 . HO$ | |
|---|---|
| Carbon . . | 66·667 |
| Hydrogen . . | 10·416 |
| Oxygen . . | 16·667 |
| Water . . | 6·250 |

| *Capric acid,* $C_{20}H_{19}O_3 . HO.$ | |
|---|---|
| Carbon . . | 69·767 |
| Hydrogen . . | 11·046 |
| Oxygen . . | 13·954 |
| Water . . . | 5·233 |

| *Cocic acid,* $C_{26}H_{25}O_3 . HO.$ | |
|---|---|
| Carbon . . | 72·90 |
| Hydrogen . . | 11·68 |
| Oxygen . . | 11·22 |
| Water . . . | 4·20 |

| *Myristic acid,* $C_{28}H_{27}O_3 . HO.$ | |
|---|---|
| Carbon . . | 73·68 |
| Hydrogen . . | 11·85 |
| Oxygen . . | 10·53 |
| Water . . . | 3·94 |

| *Palmitic acid,* $C_{32}H_{31}O_3 . HO.$ | |
|---|---|
| Carbon . . | 75·00 |
| Hydrogen . . | 12·12 |
| Oxygen . . | 9·37 |
| Water . . . | 3·51 |

| *Margaric acid,* $C_{34}H_{33}O_3 . HO.$ | |
|---|---|
| Carbon . . | 75·556 |
| Hydrogen . . | 12·222 |
| Oxygen . . | 8·889 |
| Water . . . | 3·333 |

| *Stearic acid,* $C_{36}H_{35}O_3 . HO.$ | |
|---|---|
| Carbon . . | 76·057 |
| Hydrogen . . | 12·324 |
| Oxygen . . | 8·450 |
| Water . . . | 3·169 |

| *Succinic acid,* $C_4H_2O_3 . HO.$ | |
|---|---|
| Carbon . . | 40·678 |
| Hydrogen . . | 3·390 |
| Oxygen . . | 40·678 |
| Water . . . | 15·254 |

| *Sebacic acid,* $C_{10}H_8O_3 . HO.$ | |
|---|---|
| Carbon . . | 59·406 |
| Hydrogen . . | 7·921 |
| Oxygen . . | 23·762 |
| Water . . . | 8·911 |

| *Oleic acid*, $C_{36}H_{33}O_3 . HO$. | |
|---|---|
| Carbon . . | 76·596 |
| Hydrogen . . | 11·702 |
| Oxygen . . | 8·511 |
| Water . . . | 3·191 |

| *Benzoic acid*, $C_{14}H_5O_3 . HO$. | |
|---|---|
| Carbon . . | 68·853 |
| Hydrogen . . | 4·098 |
| Oxygen . . | 19·672 |
| Water . . . | 7·377 |

| *Lactic acid*, $C_6H_5O_5 . HO$. | |
|---|---|
| Carbon . . | 40·000 |
| Hydrogen . . | 5·555 |
| Oxygen . . | 44·445 |
| Water . . . | 10·000 |

| *Cholic acid*, $C_{48}H_{39}O_9 . HO$. | |
|---|---|
| Carbon . . | 70·588 |
| Hydrogen . . | 9·559 |
| Oxygen . . | 17·647 |
| Water . . . | 2·206 |

# CHAPTER II.

## NITROGENOUS BASIC BODIES.

(30.) The organic bases are divisible into two well-marked groups, according as they contain or are devoid of oxygen; the former being, without exception, volatile; and the latter non-volatile or fixed.

Volatile alkaloids.

None of the *volatile alkaloids* have as yet been found preformed in the animal body. Trimethylamine, $C_6H_9N$, has been found amongst the products of the spontaneous decomposition of animal matters in herring-brine, putrid urine, and alcohol in which anatomical preparations have been long preserved; and some others are obtained artificially by the dry distillation of bones, gelatin, &c.

Non-volatile alkaloids.

(31.) The *non-volatile alkaloids* may be arranged in two groups.

The first group includes four crystallisable homologous bases, represented by the formula $C_nH_{n+1}NO_4$; namely,

| | |
|---|---|
| Glycine . . . . . | $C_4H_5NO_4$. |
| Sarcosine . . . . . | $C_6H_7NO_4$. |
| A substance homologous to leucine (not yet named) . . . | $C_{10}H_{11}NO_4$. |
| and Leucine . . . . . | $C_{12}H_{13}NO_4$. |

These become broken up by nitrous acid, $NO_3$, into acids of the lactic-acid group: thus, for instance, glycine yields glycic acid, in accordance with the following equation:— $C_4H_5NO_4 + NO_3 = 2N + 2HO + C_4H_3O_5$. Under the action of strong alkalies they lose two atoms of carbon and yield one of the volatile fatty acids, glycine yielding formic acid; sarcosine, acetic acid; and leucine, valerianic acid. The re-

action in the last case is expressed by the equation, $C_{12}H_{13}NO_4 + 3KO.HO = 2KO.CO_2 + H_3N + 4H + KO.C_{10}H_9O_3$.

(32.) *Glycine*, known formerly as *sugar of gelatin*, and more recently as *glycocoll*, crystallises in colourless rhombic prisms (*Plate I. fig.* 8.), which have a sweetish taste, and are devoid of odour. It is very soluble in water, the solution having no effect on vegetable colours, but does not dissolve readily in alcohol. Glycine.

It has been long known that glycine is a product of the decomposition of animal substances, especially of gelatin, when acted upon by strong acids or alkalies. Its occurrence, however, in certain animal acids as a nitrogenous adjunct, is a point of much more physiological importance; thus, for instance, conjugated with cholic acid, it occurs as glycocholic acid in the bile; and since hippuric acid, when heated with strong mineral acids, yields glycine, it is regarded by some chemists as glycobenzoic acid.

After the use of glycine the quantities of urea and uric acid are increased, but no glycine passes unchanged into the urine (Horsford).

(33.) *Sarcosine* has never been found preformed in the animal body, and is only known as a product of the decomposition of creatine when acted upon by caustic baryta. Sarcosine.

(34.) *Leucine* in a state of purity occurs in glistening colourless plates, which, when seen under the microscope, appear as rhombic tablets and prisms, or as needles arranged in star-like groups. Such is the description of the crystalline form of leucine given by Lehmann and Funke. Virchow, who has attentively studied this substance, (especially in relation to its occurrence in the pancreas,) has, however, never been able to perceive these plates, and in his examinations of leucine (both natural and artificially prepared), even with the highest powers, has only found acicular crystals. If, says Scherer*, we Leucine.

* In his Report on the Progress of Pathological Chemistry during the year 1855, in Canstatt's Jahresbericht, where this subject is very fully discussed.

allow leucine to crystallise from a solvent, we always first observe minute granules of a roundish form, which may be distinguished from fat-globules by their inferior brilliancy and their paler edges. These often combine and form either nodular or star-like masses. Different forms of the crystals, as depicted both by Funke and Robin, are given in *Pl. II. fig.* 1.

Leucine is freely soluble in water, less so in alcohol, and is insoluble in ether. Its solutions exert no influence on vegetable colours. On saturating moderately concentrated nitric acid with leucine, we obtain crystals of nitrate of leucine, or leuconitric acid, the salts of which decrepitate when heated. Its behaviour towards nitric acid, and its decomposition into valerianic acid* (see § 31), together with the observation of its crystalline form, constitute tolerably certain means of distinguishing this substance. In most of the cases in which it is reported to have been found in the animal tissues, its presence has however been established by ultimate analysis.

Leucine is obtained from numerous animal substances, in various ways. It is produced by the action of strong acids or alkalies on any of the protein-bodies, and likewise during their putrefaction; it has also been similarly obtained from elastic tissue, horn, feathers, hedge-hog spines, hair, and the elytra of the cockchafer.

Its occurrence.

Previous to the year 1853, the only fact tending to show that leucine was probably an occasional constituent of the animal body, was an isolated observation made by Liebig, who, in his "Letters on Chemistry," mentions that he has found it in the decoction of the liver of the calf. Since that period the researches of Frerichs and Städeler, of Robin, of Virchow, Scherer, Gorup-Besanez, and Cloëtta, have shown that leucine and the closely allied substance, tyrosine, have a much wider distribution than was previously suspected. It exists in the

* Leucine also is readily converted into valerianic acid, if it be exposed to the influence of a little muscular fibre or albumen in a state of putrefaction.

blood, in the vascular glands, viz., the thymus gland, the thyroid body, and the spleen, in the liver and the bile, in the pancreas and salivary glands and their secretions, in the contents of the small intestine (derived probably from the pancreatic fluid), in the lymphatic glands, in the lungs, and in the kidneys; and has been found in a diseased brain. That it actually exists as leucine in the body, and is not a product of decomposition, formed after death, is evident from the circumstances that it has been occasionally found in the urine (in disease), and that it may be obtained from the pancreatic and salivary secretions of living animals.

Leucine has been sought for unsuccessfully in the muscles.

It is in the pancreas that it occurs most abundantly.

The *lienine* discovered some years ago by Scherer in the spleen, and the *thymine*, subsequently discovered by Gorup-Besanez in the thymus gland, are now regarded by those chemists as identical with leucine.

According to Bödeker, leucine is an ordinary constituent of pus; and it was especially abundant in the pus in a case of necrosis of the upper jaw, arising from the fumes of phosphorus.

(35.) A *body homologous to leucine*, and very similar to it, has been discovered by Gorup-Besanez in the pancreas of the ox. Its formula is $C_{10}H_{11}NO_4$. He gives a table in which the properties of these two bodies are compared and contrasted, in the Ann. d. Ch. u. Pharm. 1856, vol. xcviii. p. 20.

(36.) *Tyrosine*, whose composition is represented by the formula $C_{18}H_{11}NO_6$, and which therefore does not strictly belong to this group, is in many respects so closely allied to leucine, that we shall notice it in this place. Tyrosine.

It forms white silky crystals, which are very difficult of solution in cold water, but dissolve more readily in hot water, and are altogether insoluble in alcohol and ether. It dissolves readily in alkalies and acids, from which it again crystallises unchanged on evaporation. I am not acquainted

with any delineation of the crystalline forms which tyrosine assumes; the acicular crystals, which in single or double tufts, or as spheres, are regarded by Robin and Verdeil as leucine, are supposed by Frerichs and Städeler to be tyrosine.

Piria has discovered a very delicate test for tyrosine, which is especially useful in distinguishing it from leucine, with which it is usually associated.

If we place a little tyrosine (1-12th or 1-15th of a grain is sufficient) on a watch-glass, moisten it with one or two drops of sulphuric acid, allow it to stand for half an hour, then dilute the mixture with water, saturate it when heated with carbonate of lime, and after filtering add a few drops of a solution of perchloride of iron, in which there is no free acid, we at once obtain a very rich violet colour. This is known as Piria's test.

Tyrosine is formed, along with leucine and other compounds not yet investigated, when albuminous or horny bodies are decomposed either by acids, alkalies, or putrefaction.

Tyrosine is scarcely ever found in the animal body except in association with leucine, and it almost always occurs in much smaller quantity than the latter. It has been found in the liver (in carcinomatous and atrophied states, but not in health) by Frerichs and Städeler, who regard it as a normal constituent of the pancreas and pancreatic juice of men and animals (the horse and ox), and who detected it in the urine of a woman with acute atrophy of the liver. They searched in vain for it in the spleen, salivary glands and saliva, lymphatic glands, thymus gland, thyroid body, brain, muscles, and lungs; and Gorup-Besanez was even less successful, failing to find any trace of it in the thymus, thyroid body, liver, kidneys, lungs, or spleen of the ox, and only once finding it in the pancreas. Scherer has found leucine, and *often* tyrosine, in all the human livers that he has examined, and confirms the view that it is an ordinary constituent of the pancreas.

The modes in which leucine and tyrosine are artificially prepared, indicate that they represent stages of the retrograde

metamorphoses of the albuminous tissues, acted upon probably by an animal ferment. In the case of the salivary glands and pancreas, the ferments which exist in their normal secretions are most likely the active agents.

(37.) The second group presents fewer points in common than the first. They are for the most part crystallisable substances, occurring normally as preformed constituents of the animal fluids, and are to be regarded as products of the metamorphosis of the nitrogenous tissues. In this group we place: —

| | |
|---|---|
| Creatine | $C_8H_9N_3O_4$ |
| Creatinine | $C_8H_7N_3O_2$ |
| Urea | $C_2H_4N_2O_2$ |
| Allantoine | $C_8H_6N_4O_6$ |
| (or, more correctly, | $C_8H_5N_4O_5 . HO$) |
| Hypoxanthine | $C_{10}H_4N_4O_2$ |
| Xanthine | $C_{10}H_4N_4O_4$ |
| Guanine | $C_{10}H_5N_5O_2$ |
| Myeline | ? |
| Cystine | $C_6H_6NS_2O_4$ |
| Taurine | $C_4H_7NS_2O_6$ |

Xanthine alone is not crystallisable, and xanthine and cystine are the only two substances whose formation is due to abnormal processes.

None of these bodies, with the exception of creatinine, possess decided basic properties; but we have deemed it expedient, as a matter of convenience, to throw them together in consequence of the similarity in their empirical composition and in their physiological relations.

(38.) *Creatine* forms transparent, glistening crystals, whose leading forms are shown in *Plate II. fig.* 2. It dissolves in 74·4 parts of cold water, and in boiling water in such quantity that the solution on cooling solidifies into a mass of delicate glistening needles. It is decomposed when boiled with baryta-water into urea and sarcosine ($C_8H_9N_3O_4 . 2HO = C_2H_4N_2O_2$ Creatine.

+ $C_6H_7NO_4$), but we are not justified in hence inferring that these bodies are its proximate constituents.

There is no direct test for the detection of creatine; and the methods that have been employed to obtain it from flesh and urine are too complicated to lead to trustworthy results in the hands of any but experienced chemists.

Creatine is constantly present in the juice both of voluntary and involuntary muscles. The quantity differs in the flesh of different kinds of animals, and even in different muscles of the same animal, but is always very small. Lean animals yield, relatively, more creatine than fat ones.

Its occurrence.

According to Liebig, the flesh of hens yields the largest amount of creatine, namely, 0·32%, the average quantity yielded by horse or ox-flesh being 0·07%. Gregory obtained from 0·1375 to 0·1418% of this substance from the heart of the ox, and from 0·0935 to 0·3% from the flesh of the cod-fish. Schlossberger found 0·067% in human flesh.

Verdeil and Marcet have found it in very minute quantity in the blood of oxen.

It does not exist in the liver or kidneys, but has been found by Lerch* amongst the soluble constituents of the human brain.

It is doubtful whether it is a normal constituent of the urine, although small quantities of it can usually be obtained from that fluid; there being reasons for believing that it is formed from creatinine during the process of extraction.

Verdeil and Robin have found it in the liquor amnii of a woman who died in the eighth month of pregnancy. Its presence in that fluid had been previously suspected by Scherer.

Its functions.

Although the view has been advocated that, from its occurring in the muscular juice, and from its large amount of nitrogen, creatine is an important nutritive agent, there are

* Schmidt's Jahrbücher, 1856, vol. xcvi. p. 152.

most decisive reasons for ranking it amongst the products of excretion; for, in the first place, if it could be employed with further advantage in the organism, it (or its near ally, creatinine) would not be allowed to escape by the kidneys; and, secondly, the readiness with which it becomes decomposed into unquestionable products of excretion, as creatinine, urea, and sarcosine, proves that it approximates more nearly to these substances than to albumen and fibrin.

Creatinine.

(39.) *Creatinine*, the most decided alkaloid of this class of bodies, forms colourless, glistening crystals of the form represented in *Plate II. fig.* 3. It has almost as caustic a taste as ammonia, reacts strongly on vegetable colours, is soluble in 11·5 parts of water at an ordinary temperature, and still more readily in hot water, and dissolves tolerably freely in spirit and in ether. It expels ammonia from ammoniacal salts, forms beautiful blue crystalline double salts with salts of the oxide of copper, and its watery solution, when treated with chloride of zinc, at once yields a granular crystalline precipitate, the particles of which, when seen under the microscope, are found to consist of very delicate concentrically-grouped needles.

Its occurrence.

Creatinine occurs both in the muscular juice and in the urine; in the latter fluid it occurs in greater and in the former fluid in less quantity than creatine; its amount is, however, too small to be determined quantitatively. Traces of it have also been found in the blood and in the liquor amnii.

There can be little doubt that creatinine takes its origin from creatine, for, independently of the fact that this change may be readily effected artificially, this is almost proved by the above-mentioned circumstance that these two bodies occur in an inverse ratio in the muscles and in the urine, and by the observation made by Liebig that urine which has become putrid yields no creatine, but only creatinine.

Urea.

(40.) *Urea* crystallises, when it separates rapidly from a concentrated solution, in white silky needles; when crystallised

more slowly from dilute solutions, it forms white, nearly transparent, striated four-sided prisms, whose ends are bounded by one or two oblique surfaces. (*Plate II. fig.* 4.) It is devoid of smell, of a saltish, cooling taste, dissolves readily in its own weight of water at an ordinary temperature, and even more freely in hot water; it is also soluble in 4 or 5 parts of cold and in 2 parts of warm alcohol; but is insoluble in pure ether. Its solutions exact no action on vegetable colours.

(41.) We shall confine our remarks upon the chemical reactions and combinations of urea almost entirely to points bearing upon its qualitative and quantitative detection.

Its chemical decompositions.

On boiling urea with strong mineral acids or with caustic alkalies, it takes up 2 atoms of water, and is decomposed into carbonic acid and ammonia ($C_2H_4N_2O_2 + 2HO = 2H_3N + 2CO_2$). Ragsky and Heintz employ this reaction for the determination of urea. The acid they use is sulphuric acid; the carbonic acid is given off and the ammonia separated from the sulphuric acid by bichloride of platinum; from the weight of the resulting compound, the quantity of ammonia, and therefore of decomposed urea, may be reckoned; 1 part corresponding to 0·134498 of urea. The same reaction takes place at an ordinary temperature when we mix putrefying nitrogenous matters with a solution of urea (as is seen in the ordinary alkaline fermentation of the urine excited by the mucus of the bladder), or when we heat a solution of urea in a closed tube or vessel to a temperature of from 250° to 460°. Bunsen employs this means of determining the amount of urea in a solution. He mixes it with a solution of chloride of barium, exposes the mixture to the required heat, and afterwards calculates the quantity of urea from the amount of carbonate of baryta that is formed; 1 part of carbonate of baryta corresponds to 0·4041 of urea.

By nitrous acid urea is decomposed into nitrogen, water, and carbonic acid ($C_2H_4N_2O_2 + 2HO + 2NO_3 = 6HO + 2CO_2 + 4N$). On this reaction Millon founds his mode of deter-

mination: a solution of nitrate of suboxide of mercury is dissolved in nitric acid, and added to a weighed solution of urea; on warming this mixture the nitrous acid reacting on the urea causes the evolution of nitrogen and carbonic acid, which latter gas is caught in a potash-apparatus and weighed.

If urea be mixed with a solution of the hypochlorite of soda, potash, or lime, it is decomposed into nitrogen, carbonic acid, and water. A measured quantity of the solution of urea is introduced into a glass tube, partly filled with mercury, an excess of the hypochlorite is added, and the tube is inverted: in a few seconds the urea begins to decompose, the carbonic acid is absorbed by the hypochlorite, and the nitrogen collects in the upper part of the tube. In three or four hours the decomposition is complete, and by a simple calculation we can estimate the amount of urea from the quantity of nitrogen. This method of determining the amount of urea has been suggested by Dr. E. Davy.

Combinations with oxide of mercury.

On gradually adding to a dilute solution of urea a dilute solution of nitrate of protoxide of mercury (the atomic weight of mercury being 100), and neutralising the free acid of the mixture from time to time by a dilute solution of carbonate of soda, a flocculent snow-white precipitate, which consists of 1 atom of urea combined with 4 atoms of oxide of mercury, and which is quite insoluble in water, is thrown down. If the addition of the salt of mercury and of carbonate of soda be continued alternately, as long as this precipitate is formed, a point is reached at which the addition of a drop of the alkaline solution occasions a yellow colour, from the formation of the hydrated oxide or the basic nitrate of mercury. This takes place as soon as all the urea is precipitated, when the carbonate of soda at once acts on the mercurial solution in the above-named manner. Hence, if the quantity of mercury in the test-fluid be known, we can calculate the amount of urea in the fluid by observing the quantity of test-fluid required for the complete precipitation. It is on

this reaction that Liebig bases his celebrated method of determining the amount of urea volumetrically.

Chloride of mercury (corrosive sublimate) does not throw down a precipitate from neutral or acid solutions of urea; if, however, bicarbonate of potash be added in excess, we get the previously-described white precipitate.

With chloride of sodium.

Urea and chloride of sodium form a soluble compound, which crystallises in glistening octohedra or rhombic prisms with oblique terminal surfaces. It contains one atom each of urea and chloride of sodium with two atoms of water. It is possible that urea may exist in this combination in the animal body.

There are two acids with which urea forms important compounds; namely, nitric and oxalic acids.

With nitric acid.

If we mix a somewhat concentrated solution of urea with pure and moderately strong nitric acid, the resulting compound of nitrate of urea with one atom of water of crystallisation is soon observed to separate in white glistening scales or laminæ. When the amount of urea in solution is very great, a semi-solid mass is at once formed on the addition of the acid.

On examining under the microscope the contact of nitric acid with a drop of a solution of urea, we first observe very obtuse rhombic octohedra, which, by the accumulation of particles, increase in size, and become converted into rhombic or hexagonal tablets. (*Plate II. fig.* 4.) These crystals occur isolated, or in uniformly superimposed masses.

This salt dissolves in about 8 parts of pure water, but is less soluble if the water contains a little nitric acid. It contains 48·78% of urea.

With oxalic acid.

On adding oxalic acid to a solution either of the preceding salt or of urea, we obtain a more insoluble salt, the oxalate of urea.

Tests.

Its behaviour towards nitric and oxalic acids affords us the best means of testing for this substance. In searching for it in

an albuminous fluid we should add a few drops of acetic acid, boil, and filter, by which means we remove as far as possible the coagulable matters. The residue of the filtrate should be extracted with cold alcohol, and the solution evaporated, so as to cause the chloride of sodium (taken up by the cold alcohol) to separate as much as possible in crystals: on now bringing a drop of the mother-liquid in contact with nitric acid under the microscope, we shall observe the formation of the crystals which have been already described; and from the solution of these crystals we can prepare and examine those of the oxalate.

Occurrence.

(42.) Urea is the most essential constituent of the urine, amounting to from 77 to 82% of the solid residue in man, and to considerably more in healthy carnivora. In normal human urine, which is extremely variable in relation to the amount of its water, the quantity usually varies from 15 to 38 in 1000 parts, 25 being about the average.

Daily amount.

The amount of urea excreted daily by an adult man of ordinary size, has been variously estimated by different chemists, as may be seen by reference to the subjoined analyses (by Scherer, Rummel, and Bischoff) of the urea at different ages, and in both sexes. According to Lehmann, a healthy man excretes, in 24 hours, from 22 to 54 grammes of urea, 32 grammes being about the average quantity: a good deal depends upon the weight, a man weighing 16 stones or more excreting 37 or 40 grammes, while a man of 9 or 10 stones does not excrete more than from 28 to 32 grammes.

SCHERER.

| | (1.) Girl. | (2.) Boy. | (3.) Man. | (4.) Man. |
|---|---|---|---|---|
| Age (in years) . . . . . | 3½ | 7 | 22 | 38 |
| Weight in English pounds . . . . | 35·7 | 49·2 | 137·8 | 153·7 |
| Urea in 24 hours, in grammes . . . | 12·98 | 18·29 | 27·01 | 29·82 |
| Daily urea for 1000 parts of bodily weight . | 0·79 | 0·81 | 0·43 | 0·42 |

RUMMEL.

| | (5.) Boy. | (6.) Boy. | (7.) Girl. | (8.) Youth. | (9.) Man. | (10.) Man. |
|---|---|---|---|---|---|---|
| Age (in years) . . . | 3 | 4 | 5 | 18 | 31 | 65 |
| Weight in English pounds . | 29·8 | 31·7 | 36·9 | 129·1 | 163·7 | 127·9 |
| Urea in 24 hours, in grammes | 13·57 | 15·59 | 18·22 | 36·52 | 39·28 | 19·17 |
| Daily urea for 1000 parts of bodily weight . . . | 1·03 | 1·08 | 1·08 | 0·62 | 0·51 | 0·33 |

BISCHOFF.

| | (11.) Boy. | (12.) Youth. | (13.) Girl. | (14.) Woman | (15.) Man.* |
|---|---|---|---|---|---|
| Age (in years) . . . . | 3 | 16 | 18 | 43 | 45 |
| Weight in English pounds . . | 35 | 107 | 145 | 197 | 237 |
| Urea in 24 hours, in grammes . . | 4·27 | 19·86 | 20·19 | 25·32 | 37·70 |
| Daily urea for 1000 parts of bodily weight . . . . . | 0·53 | 0·41 | 0·30 | 0·28 | 0·35 |

These analyses, on the whole, bear out Lehmann's statement regarding the influence of weight on the amount of urea (compare analyses (3), (4), and (9), ); but that the quantity of urea does not always vary directly as the weight, is shown by analysis (8).

We see from the above tables (excluding case 11, which seems to be exceptional), that for a definite bodily weight (say for instance 1000 parts) there is about three times as much urea excreted in childhood (between the ages of 3 and 7), as at the age of 65, an intermediate quantity being yielded in adult life.

The latest observations on the amount of urea excreted normally, and under various conditions, are those of Beigel. From 58 observations made on 10 healthy young men between the ages of 20 and 30, and living their ordinary

* The "man" is Bischoff himself: in 40 analyses of his own urine the maximum quantity of urea was 48·87 and the minimum 29·34 grammes.

mode of life in relation to diet and exercise, he deduces as the average amount, 35·69 grammes; and he finds that for every 1000 parts of bodily weight they yield daily 0·46 of urea, while from corresponding observations on 6 healthy young women between the ages of 19 and 30 years, he infers that the normal daily quantity of urea excreted by them amounts to 27·61 grammes, and that for 1000 parts of bodily weight they yield 0·42 of urea. Hence, he observes, women excrete daily 8·03 grammes less urea than men; but he apparently overlooks the fact that the weight of the men averaged 76·1 kilogrammes (or about 168lbs), while the mean weight of the women was only 64·5 kilogrammes (or about 142 lbs). Making due allowance for the lighter average weight of women, the smaller quantity of nitrogenous food which they usually take, and the less severe bodily exercise they undergo —and, as we shall immediately see, all these are factors in this question—there seems no evidence that sex directly influences the excretion of urea.

Influence of sex.

The influence which the nature of the food exerts on the amount of urea, is forcibly shown by Lehmann's experiments upon himself, Beigel's upon healthy young men and women, and Bischoff's on dogs. Lehmann found that on a purely animal diet, or on food very rich in nitrogen, there were often two-fifths more urea excreted than on a mixed diet; while on a mixed diet there was almost one-third more than on a purely vegetable diet; while, finally, on a non-nitrogenous diet the amount of urea was less than half the quantity excreted during a mixed diet. The following are his mean results:— On an ordinary mixed diet, 32·5 grammes; on a purely animal diet, 53·2 grammes; on a purely vegetable diet, 22·5 grammes; and on non-nitrogenous diet, 15·4 grammes. Beigel found that healthy men living on a very scanty diet (of rolls and a kind of porridge), and taking no exercise whatever (lying in bed except for three hours which were spent on the sofa), excreted only 31·86 grammes of urea, and that with strong

Of food.

exercise it rose to 33·32 grammes; and that the same persons, when enjoying a superabundant animal diet, and plenty of bottled porter, excreted, when spending the day on the sofa, 46·10 grammes, and with strong exercise, 52·26 grammes.—Hence he draws the inference that a diminution in the amount of nitrogenous food does not produce so marked an effect in causing a decrease of the urea as a superfluity of such food produces in augmenting the urea.

In two syphilitic patients (men aged 22 and 26 years), who were undergoing the so-called hunger-cure, whose urine was examined for 8 and 10 days respectively, the mean daily quantities of urea were 17·83 and 22·715 grammes.

Bischoff believes that the increase of the urea is only limited by the power of the individual to dissolve and digest nitrogenous food: one of the dogs on which he experimented, when taking nearly 9lbs of beef freed from fat and bone, discharged 190 grammes (more than six ounces) of urea daily, and while living on little more than 1lb of potatoes and half a pound of fat, excreted not more than from 6 to 8 grammes (or from a drachm and a half to two drachms).

He finds that the use of gelatin as food increases the quantity of urea to a great extent; but he believes that the additional urea is merely a product of the decomposition of the gelatin in the blood, without its having contributed to form any tissue of the body.

We are indebted to the same observer for the knowledge of the fact that common salt exerts an unquestionable influence in augmenting the excretion of urea, in consequence doubtless of its augmenting the rapidity of metamorphic action in the tissues.

The researches of Heller, Böcker, and Julius Lehmann show that alcohol, tea, and coffee (especially the empyreumatic aromatic substance contained in it) diminish the daily quantity of urea.

Of exercise.

Strong bodily exercise increases the quantity of urea very

considerably. All observers, excepting Rummel, agree on this point. Lehmann found that while during his ordinary mode of living he excreted about 32 grammes, the amount rose to 36 and even to 37·4 grammes after severe exertion. His experiments are confirmed by those of Beigel, quoted in the preceding page, who found that on a full animal diet exercise caused an augmentation of the urea amounting to 6·16 grammes.

Of medicines.

Little is definitely known regarding the power of remedial agents in modifying the amount of urea, except that Liquor potassæ has been decisively proved, by the experiments of Dr. Parkes, to increase its quantity. The experiments of Böcker, Beigel, and others on this subject, are too vague and uncertain in their results to call for special notice.

Of diseases.

Our information on the effect which diseases produce on the amount of urea is not very satisfactory. Heller observed the greatest quantity of urea in meningitis, the whole urine solidifying in a few minutes into a crystalline magma on the addition of concentrated nitric acid. According to the same observer, the urea is in excess during the stage of exudation, but diminishes during resorption, in pneumonia, in pleuritis, and in acute rheumatism, especially if endocarditis be simultaneously present: in the beginning of typhus there is an augmentation of the urea, but not so great as in the above-mentioned diseases. In most renal disorders, and in the chronic neuroses, there is a diminution of this constituent. Dr. A. Vogel, in an excellent memoir "On the Augmentation and Diminution of Urea in Diseases," which is based upon 182 analyses, conducted according to Liebig's method, states that he found the largest amount, 80 grammes, in a case of pyæmia, and the next greatest quantity, 69 grammes, in a case of typhus fever. It appears, from his investigations, that in typhus fever the excretion of urea is increased only so long as the febrile symptoms continue, and that when the fever is over the quantity of urea falls below the normal amount, not-

withstanding the increased quantity of nitrogenous food.* In Bright's disease (affecting both kidneys) the urea often falls to one-third or one-fourth of the normal quantity; and in polydipsia hysterica (although the amount of urine is very great) the total quantity of urea is much diminished. The smallest quantity observed by Vogel occurred in a case of carcinoma of the liver with great atrophy, when it was once found to fall below 7 grammes.

Its presence in blood.

It is only recently that the presence of traces of urea in healthy blood has been satisfactorily established; the rapidity with which it is removed by the kidneys, rendering its certain detection, even in five or six pounds of blood, by no means easy.† It is abnormally increased in cases in which the functions of the kidneys are imperfectly executed, especially in Bright's disease, renal ischuria, and cholera.

It is a normal constituent of the fluids of the eye (Millon, Wöhler), and of the liquor amnii (Scherer).

Urea has been in vain sought for in healthy muscular tissue, where, if the theory be correct that it is mainly formed by the disintegration of that structure, we should especially expect to find it. It has, however, been found by Buhl and Voit, and likewise by von Bibra ‡, in considerable quantity in the muscular tissue of cholera patients. In one case von Bibra found 0·317% of urea in the dried tissue of the glutæal muscles.

Whenever the urea is not duly separated by the kidneys we find it in most of the animal fluids, especially in the sweat and in serous exudations: under these circumstances it likewise occurs in lesser quantity in the saliva, the bile, and vomited matters.

* The Gulstonian Lectures of Dr. Parkes, "on Fever," published in the "Medical Times" in the Spring of 1855, contain much information on this point; indeed, they embrace the whole Chemistry of Fever.

† Since the above paragraph was written, M. Picard has shown that Liebig's volumetric method of testing quantitatively for urea may be applied to the blood, from which it will separate the smallest traces. He found in the dog that the blood of the renal artery yielded 0.0365% of urea, while that of the renal vein yielded only 0·0186%. Comp. Rend. Sept. 8th, 1856.

‡ Ann. d. Ch. u. Pharm. 1855, vol. xciv. p. 211.

(43.) It is well known that the origin of urea is still a *quæstio vexata* amongst chemists and physiologists; one party, including the names of Liebig, Bischoff, and others, holding that the urea is solely a product of the metamorphosis of the nitrogenous tissues; whilst the other party, which ranks amongst its supporters Lehmann, Frerichs, and (more especially) Bidder and Schmidt, maintain that the formation of urea is dependent upon two factors, one of which is variable, namely, the amount of assimilated histoplastic or albuminous food; while the other is constant, namely, the necessary consumption of the albuminous tissue when the animal is fasting.* Its origin.

It admits of no doubt that urea is formed from the nitrogenous constituents of the organism, its artificial production† from such substances affording the strongest evidence on that point: in addition to which we may add the facts observed by Lassaigne, Scherer, and others, of urea being contained in the urine excreted after nearly three weeks' starvation. As the metamorphosis of tissue occurs with the greatest activity in the muscular system, and as, further, increased bodily exercise augments the amount of urea, we are justified in regarding the urea as formed for the most part from the worn-out muscular fibres, although it is most

* Fuhrer and Ludwig, in a recent memoir "On the Physiological Compensation of the Spleen, and on the Sources of Urea," of which I have only seen an abstract in Schmidt's Jahrbücher, maintain a third view; namely, that the urea, during the normal nutrition of the body, especially depends on the solution of the morphotic elements of the blood (especially the hæmatocrystalline), and that all superfluous food causes an excessive formation and destruction of these elements.

† The artificial formation of urea from cyanate of ammonia is fully described in all our more recent treatises on Organic Chemistry. Its formation by oxidation, from uric acid, and allantoine, are noticed in our remarks on those substances. Dumas has recently announced (Comp. Rend. Sept. 8, 1856) that Béchamp, a young French chemist, has succeeded in transforming albumen into urea, by digesting it with a solution of permanganate of potash, at a temperature of 176° F. This result leads to the conclusion that the urea is naturally formed by a slow combustion of the albumen of the blood.

probable that other vital tissues may contribute to the general amount. Whether it is formed in the organic particles at the moment of their disintegration, or whether it is first formed in the blood, is a point which cannot be considered as decisively established; but it is most probable that the latter is the correct view, because Liebig, in his experiments on large quantities of muscular juice, could not detect in it any trace of urea, although he found substances from which he could produce it artificially. It seems, therefore, almost certain that these substances (creatine, creatinine, and probably inosic acid) are decomposed in the blood, by the action of the alkalies and of free oxygen, into urea and other matters to be excreted. Moreover, the view that the urea is formed in the blood is supported by well-known experiments, showing that gelatin, glycine, alloxantin, theine, and other substances, which it is impossible to suppose can form tissue, are converted into urea and other matters, as is evidenced by the fact that this substance occurs in a perceptibly increased quantity in the urine, soon after any of the above-named substances have been swallowed.

Lehmann's view that the urea is in part formed from assimilated nitrogenous food which has never entered into the substance of the tissues, is chiefly based on the following facts: (1.) on the extent to which its amount is increased by the free use of animal food (nature in this way getting rid of the superfluous plastic material along with that which has become unfit for use); and (2.) on the circumstance first noticed by Frerichs, but mainly established by the investigations of his opponent, Bischoff, that the use of gelatin and gelatinous food so rapidly increases the quantity of urea, that we are compelled to believe that these nitrogenous matters are at once directly oxidised in the blood, without having entered into the composition of the tissues; and if these, why not the protein-bodies also? (We should observe that Bischoff himself fully grants that the gelatin is directly converted in the blood into

urea, but, he adds, it is never a natural article of food, nor is it ever found as a normal constituent of the blood).

When treating of uric acid we shall show that in all probability a great part of the urea, separated by the kidneys from the blood, had previously existed in the form of that organic acid.

Whether urea exerts any special influence on the fluids of the eye is a question that no one has yet attempted to answer.

(44.) *Allantoine*, which is always associated with one atom of water, forms colourless, hard, glistening, four-sided prisms. (See *Plate II. fig.* 6.) It dissolves in 160 parts of cold water, and more readily in hot water: it is soluble in hot alcohol, from which it crystallises on cooling, and is insoluble in ether. Allantoine.

When exposed to the action of concentrated alkalies it takes up water, and is resolved into oxalic acid and ammonia.

Boiling nitric acid decomposes it into urea and allantoic acid, $C_{10}H_7N_4O_9$: moreover, on exposing allantoine to fermentation with a little yeast, urea is also formed in association with various ammonia-salts.

Allantoine is precipitated by nitrate of protoxide of mercury in precisely the same manner as urea: hence, if this substance were present in urine, it would interfere with the application of Liebig's method. It moreover reduces the oxide of copper: hence it would interfere with Trommer's test for sugar.

There is no special test for the detection of allantoine, but we may attach considerable weight to the determination of the form of its crystals.

This substance exists naturally in the allantoic fluid, as likewise in the urine of calves as long as they continue to suck; when they begin to take vegetable food it disappears, and is replaced by hippuric acid. Frerichs and Städeler have recently shown that it may occur in the urine in cases of impeded respiration; they found it in the urine of two dogs the action of whose lungs was artificially impeded; and there

was a doubtful trace of it in the urine of a man with disease of the respiratory organs.

It is sufficiently obvious from the positions and circumstances in which it occurs, that allantoine is a product of the metamorphosis of the animal tissues. Under certain conditions with which we are as yet unacquainted, it probably constitutes an intermediate stage in the disintegration of tissues between uric acid and urea: at all events we know that allantoine is one of the products of oxidation of the above-named acid (see § 58), and that under the influence of oxidising agents (nitric acid and yeast), it yields urea as one of its products.

Hypoxanthine.

(45.) *Hypoxanthine*, in a state of purity, exists as a crystalline powder, difficult of solution in cold water, but dissolving more readily in boiling water (1 part in 180). If its solution in nitric acid be evaporated, there remains an intense yellow residue, which when treated with potash assumes a brilliant reddish yellow colour.

This substance was discovered by Scherer in the splenic juice both of the ox and of man, and in the muscular tissue of the heart. It has subsequently been found by Gerhard (a pupil of Scherer's) in the blood of oxen, and by Scherer himself (in considerable quantity) in human blood in a case of leucæmia. Gorup-Besanez, who has carefully examined many of the glandular tissues, has not only confirmed Scherer's discovery of its existence in the spleen, but he also found it in the thymus and thyroid glands. Scherer has, during the present year (1856), announced its discovery, in association with uric acid, in varying quantities in every human liver that he has examined: and in the pancreas it is so abundant, in association with leucine and tyrosine, that he regards this gland as a good source for yielding all these bodies. Nothing can as yet be decided regarding its physiological importance.

Xanthine.

(46.) *Xanthine*, which was formerly known as uric oxide,

is not crystallisable. It is only found in urinary calculi, of which it is a very rare constituent, and nothing is known of the conditions under which it is produced.

(47.) *Guanine* occurs in the excrements of certain sea-fowl and of spiders. It has likewise been found as a glandular product in the river cray-fish and the fresh-water mussel. It receives its name from its being first discovered in guano. Guanine.

(48.) *Myeline* is a name given by Virchow to a substance which he has discovered in diseased lungs, in an hepatic cyst, in healthy and diseased spleens, &c. He has given it this name from its resemblance to the nerve-medulla. Its chemical nature seems extremely doubtful. Myeline.

(49.) *Cystine* occurs, in a state of purity, in colourless, transparent, hexagonal plates or prisms. (See *Plate II. fig.* 7.) It is insoluble in water and alcohol, but dissolves in the mineral acids (with most of which it forms salt-like compounds), in oxalic acid, in the fixed alkalies and their carbonates, and in ammonia; but not in the carbonate of ammonia. It is best thrown down from its acid solutions by carbonate of ammonia, and from its alkaline solutions by acetic acid. The peculiar form of the crystals of this substance suffices at once to distinguish it from all other bodies, excepting, perhaps, uric acid, which I have occasionally seen to assume a nearly similar shape.* Cystine.

Cystine is a rare constituent of urinary calculi. (In 129 specimens Taylor only found 2 containing it.) It has occasionally been found as a urinary sediment, mixed with urate of soda; and in such cystine-containing urine an additional precipitate may often be obtained (according to Golding Bird) by the addition of acetic acid. Virchow has recently (1856)

* That cystine occasionally crystallises in other forms than hexagonal plates is obvious, from an observation recently made by Virchow, who found a large renal calculus of cystine, composed of very acute rhombic tablets or broader rhombic prisms in a state of aggregation. Thaulow had, I believe, previously noticed this peculiarity.

obtained unquestionable evidence of the presence of cystine in the aqueous decoction of the liver of a typhus patient.

Nothing is known regarding the origin of cystine. As in his investigation of the glandular structures Cloëtta sometimes found taurine and sometimes cystine in the kidneys, he infers that the latter is formed from the former. In its chemical composition it differs from all other animal bodies, with the exception of taurine, in the enormous quantity of sulphur which it contains (26·7%); no other substances in which this element occurs, as albumen, casein, fibrin, &c., containing more than 2%. It is not impossible that when cystine occurs in the urine, the kidneys may be acting vicariously for the liver. This view is borne out by the recent observations of Virchow and Cloëtta to which we have alluded.

Taurine.

(50.) *Taurine* crystallises in colourless, perfectly transparent six-sided prisms with pointed extremities (see *Plate II. fig.* 8.); it dissolves readily in water, slightly in spirit, and is insoluble in absolute alcohol and ether. It dissolves unchanged in the mineral acids, but it neither combines with them nor with bases. Strecker has recently succeeded in forming taurine artificially from isethionate of ammonia, $NH_4O . C_4H_5O . 2SO_2$ (which $= C_4H_7NO_6S_2 + 2HO$, and, therefore, only differs from taurine by two equivalents of water), by exposure to a high temperature. (Isethionic acid is formed by the action of anhydrous sulphuric acid on alcohol with the aid of heat.*)

This substance exists preformed in the normal bile of most animals, as an adjunct to the cholic acid, which has been already described. (See § 25.) It is only in decomposed or morbid bile that it occurs in an isolated form, and thus we can account for its occasional detection in the contents of the intestines and in the excrements. After the removal of the mucus all the sulphur of the bile is due to the taurine (which contains 25·6% of that element). Cloëtta, in his investigations

* See Gregory's "Handbook of Organic Chemistry," 4th ed. 1856, p. 227.

regarding the chemistry of the glands, finds taurine in the lungs and sometimes in the kidneys. Further observations on the occurrence of taurine in the animal fluids will be found in § 55. in our remarks on taurocholic acid.

It is still a doubtful point whether taurine be actually formed in the liver, or whether that gland merely separates it from the blood in a similar manner to the separation of the urea by the kidneys; the former is the more probable view, for the reasons given in § 166. regarding the formation of the bile. Strecker's discovery renders it almost certain that the sulphur exists in taurine in an oxidised state; a view that is further confirmed by the fact that it cannot be detected by the ordinary fluid oxidising agents: hence its formation must at all events be regarded as dependent on a process of oxidation; and, as we shall subsequently see, when treating of the bile, the liver is most probably the seat of its production.

Valenciennes and Fremy, in their recent memoir "On the Composition of the Muscles in the Animal Series," found in the muscular tissue of all the molluscs that they examined a substance which, in both its crystallographic character and its chemical composition, seems to be identical with taurine; and they believe that these results will modify the view generally held, that taurine originates in the liver, and that it will be found to be much more abundant in the animal organisation than is generally supposed. The researches of Cloëtta (1856) strongly confirm this view.

(50*.) TABULAR VIEW OF THE COMPOSITION OF THE NITROGENOUS BASES.

| *Glycine*, $C_4H_5NO_4$. | | *Sarcosine*, $C_6H_7NO_4$. | |
|---|---|---|---|
| Carbon . . . | 32·00 | Carbon . . | 40·45 |
| Hydrogen . . | 6·67 | Hydrogen . . | 7·86 |
| Nitrogen . . | 18·67 | Nitrogen . . | 15·73 |
| Oxygen . . | 42·66 | Oxygen . . | 35·96 |

*Leucine*, $C_{12}H_{13}NO_4$.

| | |
|---|---|
| Carbon | 54·96 |
| Hydrogen | 9·92 |
| Nitrogen | 10·68 |
| Oxygen | 24·44 |

*Tyrosine*, $C_{18}H_{11}NO_6$.

| | |
|---|---|
| Carbon | 59·67 |
| Hydrogen | 6·08 |
| Nitrogen | 7·73 |
| Oxygen | 26·52 |

*Creatine*, $C_8H_9N_3O_4$.

| | |
|---|---|
| Carbon | 36·64 |
| Hydrogen | 6·87 |
| Nitrogen | 32·06 |
| Oxygen | 24·43 |

*Creatinine*, $C_8H_7N_3O_2$.

| | |
|---|---|
| Carbon | 42·48 |
| Hydrogen | 6·19 |
| Nitrogen | 37·17 |
| Oxygen | 14·16 |

*Urea*, $C_2H_4N_2O_2$.

| | |
|---|---|
| Carbon | 20·000 |
| Hydrogen | 6·666 |
| Nitrogen | 46·667 |
| Oxygen | 26·667 |

*Allantoine*, $C_8H_5N_4O_5$. HO.

| | |
|---|---|
| Carbon | 30·38 |
| Hydrogen | 3·16 |
| Nitrogen | 35·44 |
| Oxygen | 25·32 |
| Water | 5·70 |

*Hypoxanthine*, $C_{10}H_4N_4O_2$.

| | |
|---|---|
| Carbon | 44·13 |
| Hydrogen | 2·94 |
| Nitrogen | 41·17 |
| Oxygen | 11·76 |

*Xanthine*, $C_{10}H_4N_4O_4$.

| | |
|---|---|
| Carbon | 39·47 |
| Hydrogen | 2·63 |
| Nitrogen | 36·84 |
| Oxygen | 21·06 |

*Cystine*, $C_6H_6NS_2O_4$.

| | |
|---|---|
| Carbon | 30·000 |
| Hydrogen | 5·000 |
| Nitrogen | 11·666 |
| Sulphur | 26·667 |
| Oxygen | 26·667 |

*Taurine*, $C_4H_7NS_2O_6$.

| | |
|---|---|
| Carbon | 19·20 |
| Hydrogen | 5·60 |
| Nitrogen | 11·20 |
| Sulphur | 25·60 |
| Oxygen | 38·40 |

# CHAPTER III.

## NITROGENOUS CONJUGATED ACIDS.

(51.) Under this head we have to consider the following acids, which we divide into three groups:—

| | | |
|---|---|---|
| I. | Hippuric acid . . . . | $C_{18}H_8NO_5 . HO.$ |
| | Glycocholic acid . . . | $C_{52}H_{42}NO_{11} . HO.$ |
| | Hyocholic acid . . . . | $C_{54}H_{43}NO_{10} . HO.$ |
| | Taurocholic acid . . . | $C_{52}H_{45}NS_2O_{14} . HO.$ |
| II. | Inosic acid . . . . . | $C_{10}H_6N_2O_{10} . HO.$ |
| | Pneumic or Pulmonic acid . | ? |
| III. | Uric acid . . . . . | $C_{10}H_4N_4O_6.$ |
| | Cynuric acid . . . | ? |

The first four of these acids are placed by themselves in the first group, because they especially present the leading characteristic of conjugated acids; that is to say, when treated with concentrated acids or with alkalies, they resolve themselves into a nitrogenous body, which we regard as the adjunct, and into a non-nitrogenous acid.

Their theoretical composition.

Hippuric acid has usually been regarded as benzoic acid conjugated with glycine, because, when digested with concentrated mineral acids, it resolves itself into those two substances ($C_{18}H_8NO_5 + 2HO = C_4H_5NO_4 + C_{14}H_5O_3$); but since it has been discovered (by Strecker) that with nitrous acid it yields the benzoglycic acid noticed in the note to § 24., it seems not improbable that it is a true amide of benzoglycic acid, $H_2N . C_{18}H_7O_6$ — a view of its composition which is in full accordance with its various decompositions, the only diffi-

culty being how it can be an amide-compound and still retain acid properties. We do not yet know whether a similar relation holds good in glycocholic and hyocholic acids, which also yield glycine when treated with acids or alkalies; the ordinary view is that they are acids conjugated with glycine, the former having the theoretical formula $C_4H_3NO_2 . C_{48}H_{39}O_9$, and the latter $C_4H_3NO_2 . C_{50}H_{40}O_8$. As taurocholic acid resolves itself, when treated with acids, into taurine and choloidic acid, we regard it as cholic acid conjugated with taurine, and as being represented by the formula $C_4H_6NS_2O_5 . C_{48}H_{39}O_9$.

The second group has not been sufficiently studied to enable us to hazard an opinion regarding their theoretical composition. Even the empirical formula for pneumic acid has not yet been determined.

We have placed uric and cynuric acids together, but it is still uncertain to what group the latter acid belongs; in its chemical composition uric acid is closely allied to the two neutral bodies hypoxanthine and xanthine, as is obvious from their formulæ:

| | |
|---|---|
| Hypoxanthine . . . | $C_{10}H_4N_4O_2$. |
| Xanthine . . . . | $C_{10}H_4N_4O_4$. |
| Uric acid . . . . | $C_{10}H_4N_4O_6$; |

so that it would seem as if these three compounds represented different stages of oxidation of the same radical, $C_{10}H_4N_4$.

Hippuric acid.

(52.) *Hippuric acid* in a state of purity occurs in regular white or semitransparent rhombic prisms, with pointed extremities (see *Plate III. fig.* 1); it is devoid of odour, has a slightly bitter taste, dissolves readily in boiling water and in alcohol, and less freely in cold water and in ether; its solutions strongly redden litmus. When gently heated in a test-tube it fuses, without loss of water, into an oily liquid, which, on cooling, solidifies into a crystalline milk-white mass; on the application of a stronger heat there is produced a crystalline sublimate of benzoic acid and benzoate of am-

monia, while red oily drops are at the same time formed, which have a peculiar aromatic odour (resembling that of the Tonka-bean or new hay), solidify on cooling, and are insoluble in water, but dissolve in spirit and in ammonia: on exposing the acid to a yet stronger heat, an intense odour of prussic acid is developed, and a porous carbonaceous mass remains.

Dessaigne has made the interesting observation that hippuric acid may be artificially formed, under certain conditions, by the mutual action of chloride of benzoyl and the compound of oxide of zinc and glycine, represented by the formula $C_4H_5N_2O_4 . ZnO$. He expresses the change that ensues by the following equation:

$$C_4H_5N_2O_4 . ZnO + C_{14}H_5O_2 . Cl_2 = C_{18}H_9N_2O_6 + ZnCl_2 + HO.$$

We have already noticed the resolution of hippuric acid, when heated with strong mineral acids, into benzoic acid and glycine, and likewise the mode in which benzoglycic acid is formed from it by the action of nitrous acid.

In fermenting and putrefying fluids hippuric acid is converted into benzoic acid and other products.

The only substance with which hippuric acid is likely to be confounded is benzoic acid contaminated with pigment and other nitrogenous matters. They may, however, be distinguished by the following points: (1.) their different behaviour when exposed in a test-tube to the action of heat; (2.) their different behaviour with ether; hippuric acid is far less soluble in ether than benzoic acid, and crystallises from hot saturated solutions in needles or prisms, while benzoic acid crystallises in scales; and (3.) a microscopic examination of the form of the crystals.

When treating of uric acid we shall show how it may be distinguished from hippuric acid.

Its occurrence.

Hippuric acid occurs in large quantities in the urine of the herbivorous mammals; it does not, however, exist in the urine of the calf until it is weaned; allantoine, uric acid, and urea

being found in this fluid till the young animal has recourse to vegetable food. It is a normal constituent of human urine during a mixed or vegetable diet; but Liebig's statement that its quantity is about the same as that of uric acid is very far from being generally true. It not unfrequently happens that 8 or 10 ounces of healthy urine will only yield a few microscopic crystals, especially if food has not been taken for 12 or 15 hours. The following experiments performed by Heller, in conjunction with a friend, must be confirmed before we accept them. After determining their normal quantity of uric acid, Heller lived for a week on wheat and rye bread, and his friend solely on rye bread (of which they took as much as they needed), and water was their only drink. The uric acid soon began to diminish, and to be replaced by hippuric acid, while the quantity of urea was not materially affected. At the end of the week there was a large quantity of hippuric with a mere trace of uric acid in Heller's urine; while in that of his friend the hippuric acid completely replaced the uric acid, not even a trace remaining. During the next week, when they were living on a mixed diet (including flesh), the process was reversed; the hippuric acid vanishing and the uric acid returning more rapidly than it had disappeared. It would thus seem, in opposition to the well-known experiments of Lehmann*, that the use of a purely vegetable diet causes the disappearance of uric acid and the simultaneous abundant formation of hippuric acid.

Roussin † has ascertained that, in the case of the horse, the proportions of hippuric acid vary directly with the work, and inversely with the urea; that is to say, that over-worked horses produce much hippuric acid and comparatively little urea; and he believes that respiratory activity and the employment of muscular force transform urea into hippuric acid. This seems a most improbable view.

* These experiments are described in the chapter on "The Urine."

† Silliman's Journal, 1856, vol. xxii. p. 102.

Hippuric acid does not exist in the urine of carnivorous animals. Lehmann has found it in the renal secretion of the common European tortoise.

In various forms of disease there is a great augmentation of hippuric acid, especially in the strongly acid urine which is frequently passed in fevers and in inflammatory diseases, and in diabetic urine.

Hippuric acid (probably in combination with soda) has recently been detected in the blood of oxen and in morbid human blood.

Schlossberger has obtained unquestionable evidence of the presence of this acid in the cutaneous scales in a well-marked case of ichthyosis: this result is the more singular, since Schottin has ascertained that benzoic acid, when administered to a healthy man, appeared unchanged in the sweat, and not in the form of hippuric acid, as in the urine.

Its origin.

Nothing very definite can be stated regarding the substances from which hippuric acid is formed, or the seat of its formation. As, however, Guckelberger's experiments have shown that the nitrogenous tissues, when treated with nitric acid, yield benzoic acid and hydruret of benzoyl (oil of bitter almonds), there is every reason to believe that they yield similar products of decomposition during the gradual oxidation which they undergo in the animal body. The benzoic acid thus formed may be supposed to unite in the nascent state with glycine, which is most probably, like urea, a common product of the decomposition of nitrogenous substances.

Glycocholic acid.

(53.) *Glycocholic acid** occurs in the form of such extremely delicate white needles that when magnified 300 times

* I have adhered throughout this volume to Lehmann's nomenclature of the biliary acids. His *glycocholic acid* is Strecker's *cholic acid.* The glycocholate of soda, with an admixture of the taurocholate, seems to be equivalent to the *biline* of Berzelius, and the *bilate of soda* of Liebig, Plattner, &c. This acid was originally discovered in 1826 by Gmelin, who gave it the name of *cholic acid.*

they have scarcely any perceptible diameter. (See *Plate III. fig.* 2.) It is difficult of solution in cold water, but dissolves more readily in hot water; it is freely soluble in spirit, slightly in ether. The cold watery solution has a sweet and somewhat bitter taste, and reddens litmus.

If glycocholic acid be boiled for a prolonged time with a solution of potash or with baryta water it takes up 2 atoms of water and becomes resolved into the non-nitrogenous cholic acid, $C_{48}H_{39}O_9 . HO$, and glycine, $C_4H_5NO_4$. With sulphuric acid and sugar (or acetic acid) it yields the same reaction as cholic acid.*

Glycocholate of soda, $NaO . C_{52}H_{42}NO_{11}$, separates from its alcoholic solution, on the addition of ether, in large, glistening, white clusters of radiating needles (see *Plate III. fig.* 3.), but does not crystallise from an aqueous or spirituous solution. Glycocholate of potash behaves in a similar manner. The so-called crystallised bile is a mixture of these two salts.

It is by no means easy to distinguish the various acids of the bile and their derivatives from one another, unless we have a considerable amount of matter to work upon; their different crystalline forms, however, considerably aid us, when the substances are separated in a state of tolerable purity.

Its occurrence.

Glycocholic acid, in combination with soda, is the main constituent of ox-gall; it is, however, also found, although in smaller proportions, in the bile of most other animals, excepting in that of the pig, where it is replaced by hyocholic acid. It very soon undergoes decomposition in the intestinal canal. Its seat of formation is, most probably, the liver.

Hyocholic acid.

(54.) *Hyocholic acid* has as yet been found only in the bile of the pig, where it exists in combination with soda, potash, and a little ammonia. It is not crystallisable, and presents considerable similarity to choloidic acid. When treated with concentrated mineral acids, it yields glycine and a resinous acid; but its rational formula is not definitely determined.

* See the description of Pettenkofer's test, in § 25.

(55.) *Taurocholic acid** has never been obtained in a state of perfect purity, glycocholic acid being always more or less present. It exists as a white, perfectly amorphous, very hygroscopic, and intensely bitter powder, which dissolves readily in water and spirit, but is insoluble in ether. Its solutions have a less acid reaction than those of glycocholic acid. It dissolves fats, fatty acids, and cholesterin freely. When boiled with mineral acids, it becomes resolved, as has been already mentioned, into taurine, $C_4H_7NS_2O_6$, and choloidic acid, $C_{48}H_{39}O_9$; when boiled with alkalies, into taurine and cholic acid; and when treated with sulphuric acid and sugar, it gives the same reaction as the other essential acids of the bile. Taurocholic acid.

The alkaline taurocholates dissolve readily in water and in alcohol, but are insoluble in ether. Nitrogenous substances, as, for instance, mucus, set up a process of decomposition in solutions of alkaline taurocholates, which may be readily ascertained by the circumstance that the solutions then become precipitable by dilute acids. The products which are formed are taurine, alkaline cholates or choloidates, and probably certain combinations of these substances with taurocholic acid that had escaped decomposition.

There is no very easy test for the detection of taurocholic acid, when it is present in only a small quantity.

Taurocholic acid, in combination usually with soda, occurs in the bile of man, the ox, the fox, the bear, the sheep, the wolf, the dog, the goat, certain birds, the frog, the boa anaconda (in which animal it seems to be unassociated with any other biliary acid), and certain fresh-water fishes. Its occurrence.

It has been detected in the blood, in transudations, and in the urine in cases of suppressed excretion of bile.

* Lehmann's *taurocholic acid* is identical with the *choleic acid* of its discoverer, Demarçay, in 1838. Strecker, in his important investigations in reference to the bile, retains Demarçay's original term.

This acid soon undergoes decomposition in the intestinal canal, so that we there find taurine, free choloidic acid, &c.

Taurocholic acid, like glycocholic acid, is most probably originally formed in the liver: but we shall return to the consideration of the formation and uses of these acids when we treat of the bile.

Inosic acid.

(56.) *Inosic acid* exists in the form of a syrupy fluid, which dissolves readily in water, but is insoluble in alcohol and ether; it reddens litmus strongly, and possesses an agreeable taste of the juice of meat. The alkaline inosates are soluble in water, and crystallisable, and when heated on a platinum spatula diffuse a powerful odour of roasted meat.

It has as yet been found only in the muscular juice. Nothing is known regarding its rational formula or its mode of formation. From the great quantity of oxygen which it contains (43·7%), it must be regarded as a product of the decomposition of effete tissues.

Pneumic acid.

(57.) *Pneumic* or *Pulmonic acid* crystallises in oblique rhombic prisms, is extremely glistening, and refracts light strongly. It dissolves readily in water, is insoluble in cold but dissolves in boiling alcohol, is insoluble in ether, forms crystallisable salts with bases, and contains not only carbon, hydrogen, and oxygen, but also nitrogen and sulphur.

It appears to be a constituent of the pulmonary tissue of all mammals. Verdeil *, its discoverer, obtained about five centigrammes (about 0·8 of a grain) from the lungs of a perfectly healthy woman, who was guillotined. Morbid conditions appear to occasion an augmentation rather than a diminution of this substance; thus, a single lung, from a man with general pneumonia in its second stage, yielded rather more than the two lungs of the guillotined woman. It appears to be formed

* This acid is fully described in Robin and Verdeil's "Traité de Chimie Anatomique et Physiologique," 1853, vol. ii. pp. 460–467. Since the above paragraph was written, Cloëtta seems to have satisfactorily proved that pneumic acid is merely taurine. (See Ann. d. Ch. u. Pharm. 1856, vol. xcix. p. 296.)

in the substance of the lung itself, and probably bears much the same relation to the pulmonary tissue that creatine does to muscle. Verdeil believes that by decomposing the carbonates of the blood with which it comes in contact, it contributes very considerably to the evolution of carbonic acid, and is thus an important factor in the respiratory process. This, however, requires confirmation.

Uric acid.

(58.) *Uric acid* *, in a state of purity, occurs as a glistening white powder, or in very minute scales, whose crystalline form, at first sight, appears very variable. Uric acid, when it gradually and spontaneously crystallises from urine, appears in most cases in the whetstone form; that is to say, it forms flat tablets, which resemble sections made with the double knife through strongly biconvex lenses, or rhombic tablets whose obtuse angles have been rounded. As the urinary pigment adheres very tenaciously to uric acid, it is only rarely that these crystals are devoid of colour; and if we see a crystal of an uncommon form and of a yellow colour, the probability is that it is a crystal of uric acid. On artificially separating uric acid from its salts it usually appears in nearly perfect rhombic tablets, but occasionally in hexagonal plates resembling those of cystine; when uric acid crystallises very slowly it forms elongated rectangular tablets, or regular four-sided prisms, the latter being often grouped together in clusters; we also have barrel-shaped or cylindrical prisms, and finally saw-like or toothed crystals. (*Plate III. fig.* 4.)

Its chemical characters.

Uric acid is devoid of taste and smell, is very slightly soluble in water (1 part requiring about 15,000 parts of cold and at least 1800 parts of boiling water for its solution),

* From an examination of the salts of uric acid by Bensch (Ann. d. Ch. u. Pharm. 1844, vol. li. pp. 189–208), it appears more than probable that we should halve the formula for this acid, and that it should be expressed by $C_5H_2N_2O_3$, or $C_5HN_2O_2.HO$. This change would convert the ordinary urates occurring in urinary sediments into bi-urates, and there are strong objections to altering the nomenclature of common objects with which every student is expected to be familiar.

scarcely more soluble in concentrated hydrochloric acid than in water, and perfectly insoluble in alcohol and ether; it dissolves tolerably freely in concentrated sulphuric acid, from which it is precipitated on the addition of water. It is moderately soluble in solutions of the alkaline carbonates, borates, phosphates, lactates, and acetates, abstracting a portion of the alkali from these salts, and forming a soluble acid urate. (A solution of ordinary phosphate of soda has, as is well known, a slightly alkaline reaction; if, however, an excess of uric acid be added, there are formed urate of soda and biphosphate of soda which has an acid reaction. It is thus that Liebig explains the acid reaction of the urine.)

If uric acid and water be stirred together till a semi-solid mass is formed, and the mixture, after being brought nearly to a boiling heat, be gradually treated with peroxide of lead as long as the brown colour of the oxide continues to disappear, there are formed allantoine, urea, and oxalic acid. The allantoine and urea are in solution, and may be separated by crystallisation; and the oxalic acid is in combination with oxide of lead. The reaction may be expressed symbolically as follows:—

1 eq. uric acid ($C_{10}H_4N_4O_6$) + 2 eq. oxygen (2O) + 3 eq. water (3HO) =

1 eq. urea ($C_2H_4N_2O_2$) + 1 eq. allantoine ($C_4H_3N_2O_3$ + 2 eq. oxalic acid ($2C_2O_3$).

This decomposition is important in a physiological point of view, as explaining a probable source of the oxalic acid as well as of the urea occurring in the urine. The ingestion of uric acid, or its injection into the veins, is rapidly followed by an augmentation of urea and of oxalate of lime in the urine*; a change here takes place within the organism, similar

* Neubauer's Memoir "On the Decomposition of Uric Acid in the Animal Body," published in the Ann. d. Ch. u. Pharm. 1856, vol. 99, pp. 206—222, should be consulted in reference to this mode of formation of urea.

to that produced by the oxidising influence of the peroxide of lead.

Uric acid dissolves in moderately strong nitric acid; nitrogen and carbonic acid are evolved, and a yellow fluid remains, containing numerous products of decomposition of the acid, which do not at present concern us. On evaporating this solution to dryness there is left a reddish residue (murexide), which, if exposed to the vapour of ammonia, or moistened with a drop of an ammoniacal solution, assumes a splendid reddish purple tint. If the murexide be moistened with a little potash-solution, a beautiful bluish purple tint is evolved. These reactions are manifested when only a very minute trace of uric acid is present.

Combinations.

(59.) There are several combinations of uric acid which require notice, as occurring in the urine and in urinary and other concretions, namely, the urates of soda, potash, ammonia, and lime.

Urate of soda usually appears under the microscope in the form of globules, studded with minute acicular prisms. (See *Plate III. fig.* 5.) It is soluble in about 124 parts of boiling water.

Urate of potash crystallises in needles, and dissolves in about 75 parts of boiling water. The solution is precipitated by hydrochlorate of ammonia and the alkaline bicarbonates.

Urate of ammonia may be obtained crystallised in extremely delicate needles, but, as usually seen under the microscope, it forms globular opaque bodies, from some points of which minute spikelets project. (See *Plate III. fig.* 6.) It is moderately soluble in hot water.

The urate of lime forms a white amorphous powder, soluble in 276 parts of boiling water.

If hydrochloric, nitric, or even acetic acid be added to a solution of one of these urates, the uric acid is precipitated in a crystalline form: if the solution be very concentrated the crystals are at once separated; if, on the other hand, it be

very dilute, 30 or even 50 hours may elapse before the process is completely effected. As a general rule the larger crystals are produced in the more dilute solutions.

Tests. (60.) The crystalline form of uric acid, and its behaviour with nitric acid and ammonia or potash, are sufficient to distinguish it from all other animal substances. If we cannot decide with certainty regarding uric acid from the form of a crystal, we must dissolve it in potash, and add a minute drop of acetic acid; we shall then always obtain one of the more common forms.

Its occurrence. (61.) Uric acid is a normal constituent of human urine, in which it usually amounts to about 0·1%. It occurs in smaller quantity in the urine of carnivorous mammals, and is altogether absent (or is present in mere traces) in that of omnivorous animals (the pig) and vegetable feeders. (Its existence in the urine of the calf while still sucking has been noticed in § 51.) The urine of birds, whatever be the nature of their food, and of serpents, consists almost solely of uric acid in combination with alkalies; which is also found in a similar state of combination in the urine of tortoises, in the excrements of butterflies, beetles, &c.

The amount of uric acid in different specimens of human urine varies with the concentration of the fluid; thus Lehmann has found as much as 0·8% in very concentrated morning urine without there being an absolute augmentation of the acid in the urine of 24 hours.

The absolute quantity of uric acid excreted by an adult man in 24 hours varies, according to Lehmann, from 0·5 to 0·9 of a gramme, or from about 8 to 14 grains; it is very little affected by the nature of the food, but seems to be diminished by exercise and increased by perfect repose. Dr. Hammond* found that when taking his ordinary moderate exercise he passed daily 13·7 grains of uric acid; with increased exercise the quantity fell to 8·2 grains; and with no

* American Journal of the Medical Sciences, quoted in the "Monthly Journal of Medical Science," 1855, vol. xx. p. 249.

exercise it rose to 24·9 grains. There is an absolute augmentation of this constituent when the digestive functions are disturbed, as after the use of indigestible food or alcoholic drinks, and in disorders accompanied with severe febrile symptoms, as, for instance, acute rheumatism; in these cases the uric acid commonly separates as an amorphous granular sediment of urate of soda, when the urine cools (see *Plate III. fig.* 5.); and the nature of the sediment may be detected by the readiness with which it disappears when the fluid is warmed. An augmentation of the uric acid associated with the formation of this sediment (which, however, is sometimes only indicative of a great concentration of the urine, and not of an absolute augmentation of the uric acid) is particularly observed in all those conditions of the system which are accompanied with much disturbance of the functions of respiration and circulation; as, for instance, pulmonary emphysema, heart-diseases, enlargement of the liver, &c.

Free uric acid (*Plate III. fig.* 4.) is scarcely ever found in freshly-discharged urine; in the great majority of cases it is formed from the urate of soda after the exposure of the urine to the atmosphere, by a process of acid fermentation which is described in the chapter on "The Urine." It is in febrile urine that this change takes place the soonest, and that the crystals of uric acid are most rapidly separated.

Urate of ammonia (*Plate III. fig.* 6.) is, moreover, like uric acid, usually a product of the fermentation of the urine; it scarcely ever occurs except in urine which, by long exposure to the air, has undergone alkaline fermentation. It is only in the fresh alkaline urine of patients with chronic catarrh of the bladder, accompanied with paralysis of that viscus, that we ever find the clusters of this salt shown in the plate.

Uric acid occurs in very minute traces in the healthy blood; it is present in excess in cases of gout and Bright's disease, but its quantity is not affected by rheumatism; it has likewise been found in excess in cholera, bronchitis, pneumonia,

&c. Dr. Garrod, to whom we are chiefly indebted for our knowledge of the conditions under which an excess of uric acid occurs in the blood, recommends the following very easy mode of detecting this acid. We have merely to place a little of the serum of the blood in a watch-glass, at the bottom of which lies a fine thread, and to add acetic acid. The uric acid becomes deposited on the thread, and is easily recognised under the microscope by the form of its crystals. This test does not indicate the presence of the acid unless 1-40th of a grain be present in 1000 grains of serum, or 1 part in 40,000; and as even this quantity is always abnormal, the appearance of the crystals is conclusive as to the existence of uric acid in morbid amount. In order to use the thread-test the serum must be perfectly fresh, for the uric acid soon decomposes, oxalic acid being probably one of its products.

Uric acid, in combination doubtless with an alkali, is a normal constituent of the aqueous extract of the spleen (Scherer, Gorup-Besanez, Cloëtta), of the liver (Scherer, Cloëtta), of the lungs (Cloëtta), and of the brain (Lerch).

It has been stated that uric acid, in the form of an alkaline urate, has been found in the sweat in cases of gout; but this cannot be regarded as an accepted fact.

Dr. Garrod has found uric acid in pericardial and peritoneal effusions, and in the fluid of a blister, in cases in which the blood contained an abnormal amount of this substance.

Urate of soda in a crystallised state usually occurs abundantly in the gouty concretions commonly designated *chalk-stones.*

Its origin.

(62.) Uric acid, like urea, must be regarded as essentially a product of excretion, but we are ignorant of the exact seat of its formation. Analyses of human urine show that generally the uric acid and the urea stand in an inverse ratio to one another in the same individual; that is to say, that when the uric acid is increased, there is a corresponding diminution of the urea (see, for example, the experiments of Ham-

mond *); moreover, the experiments of Wöhler and Frerichs, and more recently of Neubauer, show that when large doses either of uric acid or of urate of potash (30 to 40 grains), were given to animals with their food, or injected into their veins, no uric acid could be detected in their urine, but there was an excess of oxalate of lime and urea, the latter exceeding the normal quantity at least fivefold. We thus have tolerably strong evidence that the greater portion of the uric acid in the animal organism undergoes a process of oxidation similar to that which can be artificially induced by peroxide of lead. Assuming, then, that the urea, or that a portion of it, is produced from uric acid, by the partial oxidation of the latter, any impediment to this process must cause less urea and more uric acid to be separated by the kidneys; and hence we see why the amount of uric acid in the urine is increased in fevers and in disturbed conditions of the circulating and respiratory functions generally. Uric acid must be regarded as a substance which stands one degree higher than urea in the retrograde metamorphosis of tissue.

Cynuric acid.

(63.) *Cynuric acid* is a crystalline acid recently discovered in small quantity, by Liebig, in the urine of dogs, and which seems to take the place of uric acid. He was only able to obtain it in a comparatively small number of cases. It has not yet been submitted to ultimate analysis.

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(64.) TABULAR VIEW OF THE COMPOSITION OF THE NITROGENOUS CONJUGATED ACIDS.

| *Hippuric acid*, $C_{18}H_8NO_5 . HO$. | | *Glycocholic acid*, $C_{52}H_{42}NO_{11} . HO$. | |
|---|---|---|---|
| Carbon . . | 60·335 | Carbon . . | 67·097 |
| Hydrogen . . | 4·469 | Hydrogen . . | 9·032 |
| Nitrogen . . | 7·821 | Nitrogen . . | 3·011 |
| Oxygen . . | 22·347 | Oxygen . . | 18·925 |
| Water . . | 5·028 | Water . . | 1·935 |

* Op. cit.

| *Hyocholic acid*, $C_{54}H_{43}NO_{10}$. | |
|---|---|
| Carbon . . | 70·28 |
| Hydrogen . . | 9·33 |
| Nitrogen . . | 3·04 |
| Oxygen . . | 17·35 |

| *Taurocholic acid*, $C_{52}H_{45}NS_2O_{14}$. | |
|---|---|
| Carbon . . | 60·58 |
| Hydrogen . . | 8·74 |
| Nitrogen . . | 2·72 |
| Sulphur . . | 6·21 |
| Oxygen . . | 21·75 |

| *Inosic acid*, $C_{10}H_6N_2O_{12}.HO$. | |
|---|---|
| Carbon . . | 32·787 |
| Hydrogen . . | 3·279 |
| Nitrogen . . | 15·300 |
| Oxygen . . | 43·716 |
| Water . . | 4·918 |

| *Uric acid*, $C_{10}H_4N_4O_6$. | |
|---|---|
| Carbon . . | 35·72 |
| Hydrogen . . | 2·38 |
| Nitrogen . . | 33·33 |
| Oxygen . . | 28·57 |

# CHAPTER IV.

## HALOID BASES AND SALTS.

(65.) THERE are three groups of haloid bases which require notice from their connection with animal chemistry. Haloid bases.

1. Those represented by the formula $C_nH_{n+1}O$, and including

| | |
|---|---|
| Oxide of doegling . . . . . | $C_{24}H_{25}O$, |
| Oxide of cetyl . . . . . | $C_{32}H_{33}O$, |
| Oxide of cerotyl . . . . . | $C_{54}H_{55}O$, |
| and Oxide of melissyl . . . . | $C_{60}H_{61}O$. |

2. Those represented by the formula $C_nH_{n-1}O$. The only base of any physiological interest pertaining to this group is the hypothetical oxide of lipyl, $C_3H_2O$.

3. The members of the group represented by the formula $C_nH_{n-7}O.HO$. We are at present only acquainted with

| | |
|---|---|
| Hydrated oxide of phenyl . . . | $C_{12}H_5O.HO$, |
| and Hydrated oxide of tauryl . . . | $C_{14}H_7O.HO$. |

(66.) The existence of *oxide of doegling* is still somewhat problematical. Scharling believes that it exists in combination with doeglingic acid in the fat of *Balæna rostrata.*

*Oxide of cetyl* is found only in spermaceti in combination with cetylic acid.

*Oxide of cerotyl,* known also as cerotin, occurs chiefly in Chinese wax in combination with cerotic acid.

*Oxide of melissyl,* formerly known as myricin, occurs in ordinary wax.

The three last named bodies, in combination with an atom of water, occur as solid, but easily fusible, white, wax-like substances.

Oxide of lipyl.

(67.) *Oxide of lipyl*, though a hypothetical body, is of far more importance than any of the preceding bases. It is well known that if we boil a fat or fatty oil with an alkali and water, the fat is decomposed into one or more fatty acids (which combine with the base that has been employed, forming soaps), and a peculiar sweet matter, glycerine. In this process there is no assimilation of oxygen or evolution of hydrogen, but the resulting products exhibit an augmentation of weight from the assimilation of water.

It was formerly assumed that the fats were combinations of the fatty acids with glycerine, whose formula was supposed to be $C_3H_2O$; but the constitution of glycero-sulphuric acid proves that glycerine must be represented by the formula, $C_6H_7O_5 . HO$, and that consequently it cannot be regarded as the base of the neutral fats. Hence it is probable that the fats contain, in adition to the fatty acid, the oxide of a radical having the composition which was formerly ascribed to glycerine; and that this oxide, in its separation from the fatty acid, takes up water, and is converted into glycerine. To this hypothetical radical Berzelius gave the name of *lipyl*.

Two atoms of oxide of lipyl, taking up four atoms of water, may be supposed to form one atom of glycerine ($2C_3H_2O + 4HO = C_6H_7O_5 . HO$). According to this theory the fats must be regarded as salts, formed by the union of the fatty acids with the oxide of lipyl.

Glycerine.

(68.) *Glycerine* is a faintly yellow fluid, with an agreeable sweet taste; it dissolves readily in water and alcohol, but not in ether, and exerts no action on vegetable colours.

Glycerine, in the form of glycero-phosphoric acid, or acid phosphate of glycerine ($C_6H_7O_5 . 2HO + PO_5$), has recently been discovered by a French chemist, Gobley, in the yolk of the egg, both in birds and fishes, and in the brain-fat, in combination with ammonia.

There can be no doubt that the origin of the glycerine in the animal body must be referred to the neutral fats; but since many fatty acids, either free or in combination with alkalies, are found in tolerable abundance in the organism, while the fats, which are taken in considerable quantity with the food, are neutral, and therefore yield glycerine, it is obvious that there must be much glycerine to be accounted for, besides the small quantity which exists in combination with phosphoric acid. We know that when glycerine that has been diluted with water is mixed with yeast and exposed to a temperature of 70° or 80° it is converted into metacetonic acid; it is not impossible that a similar change may occur in the body, the metacetonic acid being burned in the blood as soon as it is formed.

The Fats.

(69.) The true neutral *Fats* or *Salts of oxide of lipyl* now claim our consideration. The properties of these fats are extremely similar to those of the fatty acids already described. Most animal fats are soft and greasy at an ordinary temperature, although some are firm and waxy, and a few liquid. They are insoluble in water, but most of them dissolve in boiling alcohol, from which they again separate on cooling, and all of them are freely soluble in ether and in volatile oils. They are colourless or yellowish, devoid of taste and odour (when fresh), float on water, render paper or linen transparent, fuse below the boiling point of water, and solidify, when their alcoholic solutions are exposed to great cold, in white nacreous scales or plates. On exposure to the air they absorb oxygen, evolve volatile acids, and become rancid. They are inflammable, and burn with a bright flame. When strongly heated they evolve the pungent odour of acrolein from the decomposition of their base.

Albuminous substances, in a state of putrefaction, and fresh pancreatic juice, act as ferments, and resolve the fat into glycerine and the corresponding fatty acid, in the same manner as sugar is resolved by yeast into alcohol and carbonic acid.

(70.) The fats occurring in the animal body are usually mixtures of various compounds of fatty acids with oxide of lipyl. Thus, human fat, according to the recent investigations of Heintz *, is a mixture of the stearate, palmitate, and oleate of oxide of lipyl; while, according to the former and more generally received view, it consists of margarate and oleate of oxide of lipyl; the solid fat of herbivorous animals consists of a mixture of various salts, in which the stearates very much preponderate; while butter contains oxide of lipyl in combination not only with margaric and oleic acids, but with an extensive group of volatile fatty acids (see § 246. in the chapter on "The Milk").

Human fat.

Stearin.

(71.) The following are the most common of the oxide-of-lipyl compounds:—

*Stearate of oxide of lipyl*, or *Stearin*, occurs as a white mass. It separates from a hot alcoholic solution, on cooling, in glistening scales, which, when seen under the microscope, are chiefly found to be nearly perfect squares (being rhombs, with

* Heintz has been for many years actively engaged in the examination of the fats, and has thrown their chemistry into a sad state of confusion. In a Memoir "On the Composition of Human Fat," published in vol. lxxxiv. of Poggendorff's "Annalen," and translated in an abridged form in the fifth volume of the "Quarterly Journal of the Chemical Society," he maintains that human fat is a mixture of at least *six* different fats; namely, stearophanin (a fat discovered by Francis in the berries of cocculus indicus); anthropin (a new substance, whose acid is represented by the formula $C_{34}H_{32}O_4$); margarin; palmitin (which is more abundant than any of the preceding ones); olein; and another fat (to which he does not assign a name), which coexists with olein in the liquid portion of the fat, but which on saponification yields an acid whose baryta-salt differs essentially from oleate of baryta.

In a subsequent memoir in vol. lxxxvii. of Pogg. Ann. we find these views materially modified; for there we find him holding:—

1. That his *anthropic acid* is only a mixture of about seven parts of palmitic acid with five of stearic acid.

2. That *margaric acid* is only a mixture of about ten parts of palmitic acid with one part of stearic acid; and

3. That the solid part of human fat consists solely of two fats, namely, of stearin and palmitin, in which the latter strongly predominates. See his "Zoochemie," pp. 383–523, and 1067-1080.

angles of 90° 5′); sometimes, however, short rhombic prisms (thick rhombic plates) are observed. (*Plate IV. fig.* 1.) It fuses at 143°6. On saponification it yields glycerine and stearic acid.

(72.) *Margarate of oxide of lipyl*, or *Margarin*, is less solid than stearin, and crystallises from hot alcohol as a white flocculent powder, which, under the microscope, appears in the form of very delicate needles, which are so grouped as to radiate from one point, and thus to form a whorl of fine capillary threads. (See *Plate IV. fig.* 2.) It fuses at 118°4. On saponification it yields glycerine and margaric acid. Margarin.

(73.) *Oleate of oxide of lipyl*, or *Olein*, is a colourless oil, which remains fluid at as low a temperature as 24°, becomes rancid on exposure to the air, is never entirely free from margarin and stearin, but yields on saponification, in addition to glycerine and oleic acid, a much larger quantity of margaric acid than can be supposed to be derived from the decomposition of the margarin. Olein.

In the detection of free (that is to say, non-saponified) fats the microscope is of more service than any chemical test. When seen under a moderate power the fat appears in drops or globules, or in true fat-cells which may be of a spherical, or oval, or a polyhedric form. These fat-cells occur in varying quantities in the connective tissue, forming the base of the corium and surrounding the muscles, being most abundantly found under the skin of the palm of the hand and the sole of the foot, and between the different glutæal muscles. The globules of free fat are shown in *Plate IV. fig.* 3., and present so characteristic an appearance that when they have been seen a few times they can hardly be confounded with anything else.

(74.) Fats occur both in the animal and the vegetable kingdoms; they are found in almost all parts of most animals, it being only in the lowest classes that fat is entirely absent. Occurrence of fat.

In connection with the human body (and the same remarks

apply to most mammals) we find a special fatty tissue (the cellular tissue of the older writers) immediately beneath the skin, in which the fat occurs in the above-mentioned cells. There are some organs, as, for instance, the orbit and the intervals between the muscles of the face, in which the fatty tissue must be regarded as a necessary and integral constituent, inasmuch as it does not disappear even in the latest stages of wasting diseases. The largest quantities of fat are found in the omentum, around the kidneys, and in the female breasts; while the smallest quantity, and occasionally not a trace, of fat is to be found in the pulmonary tissue, the glans penis, and the clitoris, and, if we except the so-called non-saponifiable fats, in the brain.

The marrow of the bones consists almost solely of fat rich in olein.

There is scarcely any animal fluid (probably none except the urine) in which larger or smaller quantities of fat cannot be recognised. It is most abundant in the yolk-fluid, where it often amounts to more than 21%. In pus it usually amounts to 5%, and in milk to about 3·5%. The chyle also is moderately rich in fat, especially after the use of fatty food, when this constituent sometimes rises to 3%. In the blood and lymph the fat is for the most part saponified and dissolved, and not in a free, suspended state, as in the preceding fluids. It is only in special conditions that we find free unsaponified fat in suspension in the blood, as, for instance, shortly after the use of fatty food, not unfrequently in cases of pregnancy, but most commonly in drunkards with granular liver.

The solid excrements sometimes contain a large quantity of free fat; this is especially observed after the excessive use of fatty foods, particularly if diarrhœa be present, or if, for any reason, the flow of bile into the intestine be impeded.

Certain organs, as the liver and spleen, and to a less extent the kidneys, always contain more or less fat (either free or enclosed in cells) in their normal state. In morbid conditions,

especially in the state of fatty degeneration, the fat accumulates in large quantities in these organs. We likewise meet with pathological deposits of fat in paralysed muscles, in the heart (in fatty degeneration), and in encysted tumours, lipoma, &c. The formation of fat is in these cases apparently due to a retrograde metamorphosis of the protein-compounds.

The quantity of fat in the human body varies considerably at different periods of life. In the earlier periods of fœtal existence we find scarcely any fat; in new-born children there is usually a considerable quantity of this substance deposited under the skin; and the organism continues rich in fat during childhood. It diminishes with the development of the sexual functions, although it again increases about middle life, and then occasionally acquires an excess never observed at any other age. In extreme old age the fat is sometimes almost completely absorbed. The female organism generally contains more fat and exhibits a greater tendency to fatty depositions than the male. The influences exerted by excessive activity of the sexual functions, by great muscular exercise, by food, temperament, &c. on the amount of fat, are too well known to require special notice.

Its origin.

(75.) The origin of the fat in the animal body must, undoubtedly, be chiefly referred to the fat taken with the food; it has, however, been established by the most careful statistico-chemical investigations on milch cows, on various animals submitted to the process of fattening, on bees fed with cane-sugar or with honey containing scarcely any wax, and on the insects inhabiting galls*, that the animal, like the vegetable, organism has the power of forming or producing

* See the observations of MM. Lacaze-Duthiers and Riche, in the second volume of the fourth series of the "Annales des Sciences Naturelles." They have examined the composition of the galls and of the larvæ of the cynips inhabiting them, and have incontestably proved that the fat which abounds in these larvæ is produced from the starch which forms the interior of the gall in which the animal lives.

fat. In these experiments far more fat was found in the body of the animal than could be referred to the fat taken with the food, and hence the excess must have been formed either from the carbo-hydrates (sugar, starch, &c.), or from the nitrogenous protein-bodies (fibrin, albumen, &c.) which had been consumed. We shall postpone the consideration of the arguments that may be advanced in favour of these two views till we treat of the metamorphosis of tissue generally; and will at present only remark that we are still entirely ignorant of the process by which fat is produced from either of these sources, and of the exact seat of its formation.

Uses of fat. (76.) The physiological value of the fats is due partly to their physical and partly to their chemical characters.

The uses of the fat deposited in the subcutaneous areolar or connective tissue are almost entirely of a physical nature; by causing a uniform diffusion of pressure through the whole adipose tissue it protects the body from blows or other external shocks. The body is further guarded from injury in leaping and falling by the fatty masses which penetrate the joints and are known as the Haversian glands; and the layers of fat on the soles of the feet and on the tuberosities of the ischia have a similar object.

Another physical use of fat is to promote the mobility of the muscles and other organs. Hence fat is found to remain the longest in the parts where motion is most needed, as in the heart, the orbit of the eye, and in the abdominal cavity.

Another important physical property of fat is that of rendering other bodies supple and diminishing their brittleness. In this point of view the utility of fat is very conspicuous in the bones.

Fat is, moreover, a very bad conductor of heat, and hence the layer of this substance beneath the skin materially checks the loss of free heat by radiation. This use of fat is most clearly seen by a reference to some of the lower animals which are exposed to a very low temperature. In the common

seal the whole of the fat is collected in the subcutaneous areolar tissue, where it forms a layer of nearly half an inch in thickness, and a similar arrangement is observed in the cetacea.

The first of the chemical uses of the fat to which we shall advert is its power of exciting and supporting the animal heat. In the oxidation of the fats in the animal organism, whether the process be gradual or rapid, a large amount of heat must of necessity be liberated; and that they are oxidised and, for the most part, ultimately reduced to carbonic acid and water, is evident, because they neither appear in any quantity in the excretions nor accumulate beyond a certain point in the organism.

Fat is one of the most active agents in the metamorphosis of animal matter. Lehmann ascertained, in experiments on lactic fermentation, that the process cannot be excited in saccharine or amylaceous fluids by albuminous bodies, excepting with the co-operation of fat; he likewise found that a certain, although a small, quantity of fat was indispensable to the metamorphosis and solution of nitrogenous food during gastric digestion — a fact which has received confirmation from the observation that, in experiments on artificial digestion, the solution of substances used as food is considerably accelerated by the presence of a little fat. The occurrence of fat in the egg, in pus, in all plastic exudations, and in all highly cellular organs, is a clear indication that this substance plays an important part in the process of cell-formation; and no animal cell or cell-yielding plasma has ever been observed into which fat does not enter as a constituent.

Lastly, a portion of the fat which is taken with the food is applied to the formation of the bile. The chemical arguments in favour of the view that the resinous acid of the bile, cholic acid, is formed from fat, are already given in § 28, in our remarks on the origin of that acid. Various physiological facts may also be adduced in support of this opinion.

Thus, when animals are starved for any length of time, the gall-bladder is found to be perfectly full, and there is a free discharge of bile from the liver. Under these circumstances, from whence can the liver draw the carbonaceous materials from which the bile is formed, unless from the fat, which disappears with great rapidity? Indeed, it has been clearly demonstrated, by the experiments of Bidder and Schmidt*, that, in animals which are being starved, the amount of bile, secreted daily, diminishes in nearly the same proportion in which the fat of the body disappears. They likewise found, by corresponding observations on similar animals, with and without artificial biliary fistulæ, that the former animals, in whom the bile escaped externally, and, therefore, did not again enter the circulation to be consumed there, constantly evolved less carbon from the lungs (in the form of carbonic acid) than the latter; and they further demonstrated, by a comparison of the inspired oxygen with the expired carbonic acid, that the missing carbon actually pertained to the fat, and to no other substance. These and other similar observations suffice to establish the fact, that the fats contribute essentially to the formation of bile; and, were it necessary, numerous pathological phenomena might be adduced as corroborative evidence.

(77.) From the consideration of the oxide of lipyl and its salts we proceed to that of the third group, which presents scarcely any basic properties; indeed, the members of it have, till very recently, been classed amongst the acids, and termed the phenylic-acid group.

Phenylic acid.

*Hydrated oxide of phenyl*, known also both as phenylic and carbolic acid, is a colourless, transparent, oily liquid, with a burning taste and the odour of creosote, to which it bears a great general resemblance. It is slightly soluble in water, but dissolves freely in alcohol and ether, its solutions having no effect on litmus paper. The only reaction that we need

* Verdauungsäfte und Stoffwechsel, 1852, pp. 386-395.

notice is that with the persalts of iron, to which it communicates a blue tint, like salicylous and salicylic acids. It was originally obtained as a product of the dry distillation of oil of coal-tar.

This acid exerts so poisonous an action on the animal organism that, *à priori*, we should deem its occurrence there highly improbable. Wöhler has, however, established the fact of its existence in castoreum in association with benzoic and salicylic acids; and Städeler regards it as a normal constituent of the urine of the cow: it is, however, most probably only a product of the decomposition of that fluid, formed during his treatment. It has been maintained that it occurs in the urine (in association with salicylous and salicylic acids) after the ingestion of salicine; but although it is doubtless yielded in considerable quantity by the distillation of that fluid, it has been established, by the investigations of Ranke, that it does not exist there in a preformed state. If the observations of Petters (of whose skill as a chemist I know nothing) are to be relied on, inunction with tar ointment seems to occasion the presence of carbolic acid in the urine.*

*Hydrated oxide of tauryl*, or taurylic acid, closely resembles the preceding substance in its general chemical characters; and, like it, it has been found by Städeler amongst the products of distillation of cows' urine. Taurylic acid.

## LIPOIDS.

(78.) This term is now applied to those bodies which were formerly called non-saponifiable fats. In many of their physical characters they resemble the true fats or salts of oxide of lipyl, but they differ essentially from them in their chemical composition and in the products of their decomposition. Lipoids.

* An abstract of his Memoir may be seen in Schmidt's Jahrbücher, 1855, vol. lxxxviii. p. 158.

The bodies pertaining to this class are:—

| | |
|---|---|
| Cholesterin . . . . | $C_{28}H_{24}O$ |
| Castorin . . . . . | ? |
| Ambrein . . . . . | ? |
| Serolin . . . . . | ? |

Cholesterin.

(79.) *Cholesterin* separates from an alcoholic solution in white, nacreous scales, which, under the microscope, are seen to be very thin and almost transparent rhombic tablets, whose angles are 100° 30′ and 79° 30′ respectively. In many of the tablets the edges and angles are more or less irregular. It is devoid of taste and smell, is perfectly neutral, fuses at 293°, is perfectly insoluble in water, but dissolves in boiling alcohol from which it crystallises on cooling, in ether, in fatty oils, and to a certain degree in taurocholic acid.

The microscope affords the best means of testing for cholesterin; if by its insolubility in water, acids, and alkalies, and by its solubility in alcohol and ether, it has been ascertained to be a fatty matter, it may be easily distinguished from all other similar substances by a measurement of its angles. The tablets are often so thin that their outline cannot be easily traced, unless we partially shade the field of the microscope. (*Plate IV. fig.* 3.) When the cholesterin occurs in solution, as in fluids containing oil or bile, it is not always very easy to obtain it in a crystalline form.

Its occurrence.

Cholesterin is a normal constituent of the bile, in which it exists, however, in very small quantity. In healthy bile it is held in solution by the taurocholic acid (or taurocholate of soda), but in partially decomposed bile, or (possibly when it occurs in abnormal quantity) we find it deposited in its crystalline form. It is the main constituent of most biliary calculi.

It is also a normal constituent of the blood, the quantity in which it occurs varying from 0·0025 to 0·02%, the average being 0·0088%. The cholesterin increases in the blood in old age and in acute inflammatory diseases.

Cholesterin is constantly found in considerable quantity in the brain, spinal chord, and nerves. Lehmann once found the choroid plexus completely encrusted with crystals of cholesterin.

It appears to be an integral constituent of normal pus, and, when that fluid becomes acid, beautiful tablets of this substance may be observed on a microscopic examination. It has, moreover, been found in large quantity in dropsical exudations, especially in the fluids of ovarian dropsy and of hydrocele; in exudations, especially in obsolete tubercle, old echinococcus cysts (such as are sometimes found in the liver), and in the ovaries and testes in certain forms of disease. It has likewise been observed on the inner coat of arteries that have undergone atheromatous degeneration, in various kinds of tumours, and in the crystalline lens in cases of cataract.

The cholesterin which is often found in the solid excrements takes its origin in the bile. It occurs abundantly in the meconium. Traces of it have been found in urine.

Nothing is known regarding the origin of cholesterin; but, from the positions in which it occurs, we may conclude that it is a product of excretion. Much as it resembles the fats in its physical and some of its chemical characters, we cannot suppose that it is derived from them, since the fats are oxidised in the animal body, whereas to form cholesterin they must undergo a process of deoxidation. Its origin.

(80.) *Castorin* and *ambrein* are crystallisable lipoids occurring in castoreum and amber respectively. Their chemical constitution is not accurately known, and they are of little physiological importance. Castorin and ambrein.

(81.) *Serolin*, which was discovered by Boudet in the solid residue of the serum of the blood, appears, from the researches of Gobley*, to be nothing more than a mixture of the crystallisable fats contained in that fluid, with a little albumen. Serolin.

* Journ. de Chim. Méd. 1851. p. 579.

# CHAPTER V.

## THE CARBO-HYDRATES.

The carbo hydrates.

(82.) THE substances belonging to this class have received the name of carbo-hydrates, because, in addition to carbon, they contain hydrogen and oxygen in the same ratio as these elements are contained in water; moreover, the number of atoms of carbon in them appears to follow a general law, since, in all the formulæ which as yet have been well established, it is divisible by 6.

Various as are the physiological properties of these bodies, they closely resemble one another in their products of decomposition as well as in other chemical points of view. They are neutral, have very little tendency to enter into combination with other bodies, and, in the few cases in which they do so, they combine in several proportions, so that it is difficult to determine their atomic weights with certainty. They are all decomposed by heat, yielding acid volatile products and inflammable gases, in addition to aqueous vapour. By digestion with dilute mineral acids most of them are converted into grape-sugar. These bodies arrange themselves into four well-known natural groups, the sugars, gums, starches, and woody fibre or cellulose; but, in relation to zoo-chemistry, we need only notice the following individual members of these groups: —

| | |
|---|---|
| Grape-sugar or glycose . . | $C_{12}H_{12}O_{12} + 2HO$ |
| Milk-sugar . . . . . | $C_{12}H_{12}O_{12}$ |
| Inosite or muscle-sugar . . | $C_{12}H_{12}O_{12} + 4HO$ |
| Paramylon . . . . . | $C_{12}H_{10}O_{10}$ |
| Cellulose . . . . . | $C_{12}H_{10}O_{10}$ |

(83.) *Grape-sugar*, known also as glucose (which ought to be written *glycose*) and diabetic sugar, crystallises with 2 atoms of water in wart-like masses, consisting of minute rhombic plates, arranged in a cauliflower form. It is white, devoid of odour, and not so sweet as cane-sugar, but sweeter than milk-sugar. It dissolves in 1·5 times its weight of cold and far more readily in hot water; it is also soluble in spirit, and to a lesser extent in absolute alcohol, but is insoluble in ether. It is directly fermentable; that is to say, in the presence of yeast, and at a mean temperature, it undergoes direct conversion into alcohol and carbonic acid ($C_{12}H_{12}O_{12} = 2C_4H_5O.HO + 4CO_2$). In contact with nitrogenous bodies, and especially with casein, it undergoes the lactic and subsequently the butyric fermentation. Its aqueous solution turns the plane of polarisation of a ray of light to the right.* Like cane-sugar it forms compounds with potash, lime, and oxide of lead, to which the term *saccharates* † has been applied; it likewise forms a very beautiful crystalline compound with chloride of sodium. Grape-sugar, or glycose.

The behaviour of this variety of sugar towards different reagents has been very fully studied. We shall here only notice a few of those reactions on which the most trustworthy tests are based.

(84.) If a solution of glycose be treated with a little solution of potash, and a few drops of a solution of sulphate of oxide of copper be then added, there is either no precipitate, or, if one be formed, it redissolves, leaving a beautiful blue fluid: on warming this fluid it assumes an orange colour, becomes turbid, and finally deposits a yellowish red precipitate of suboxide of copper. This is Trommer's test. When the Trommer's test.

* In the following pages I have not referred to the polarisation test, because the expense of the apparatus excludes it from general use.

† A very bad term, since there is a saccharic acid formed by the action of dilute nitric acid on sugar. Potash-sugar, lime-sugar, &c., are terms more in accordance with our present rules of nomenclature.

sugar is present in only very small quantity, it is advisable to evaporate the fluid to dryness, to extract the solid residue with alcohol, to dissolve this extract in water, and then to apply the potash and sulphate of copper to this solution. By this course we usually obtain the reaction in its most distinct manner. If there is any probability that albuminate of soda be present, we must neutralise the fluid, previous to its evaporation, with a few drops of dilute acetic acid, which will prevent any albuminous body from being taken up by the alcohol. If the reaction do not fully manifest itself in the alcoholic extract thus obtained, we may precipitate the sugar from the alcoholic solution by an alcoholic solution of potash, dissolve the compound of sugar and potash (the so-called saccharate of potash, or potash-sugar, which occurs in white viscid flakes) in water, and now apply the sulphate of copper. In this way an extremely minute trace of sugar may be beautifully exhibited.

The following precautions should be attended to in the application of Trommer's test:—(1.) If the potash gives rise to a copious precipitate, the solution should be filtered before the addition of the sulphate of copper. (2.) The sulphate of copper must be added gradually and in a dilute state, because the quantity of oxide of copper that can be dissolved is proportional to the amount of sugar which is present. (3.) Prolonged heating must be avoided, for there are several animal matters (amongst which we may name the albuminous bodies) which by very prolonged boiling separate a little suboxide of copper from alkaline solutions of oxide of copper. Indeed, when sugar is present, a red or yellow powder of suboxide of copper is usually formed, even without the application of heat, if the blue solution be allowed to stand for some time.

With due attention to the above precautions, this is the most trustworthy test for sugar that we possess.

Moore's test.

85. On boiling a fluid containing grape-sugar with a solution of potash, the mixture gradually assumes a brownish red

or bistre tint, and on then adding a drop or two of nitric acid a pungent odour, somewhat resembling that of burnt sugar, is developed. This reaction, which has been long known in so far as the change of colour is concerned, is sometimes designated as Moore's test; the discovery of the peculiar odour that is evolved on the addition of nitric acid is due to Heller.

Maumené's test.

(86.) A test which is very delicate, but which unfortunately applies equally to all the carbo-hydrates, has been recently proposed by Maumené. If a pure woollen tissue (merino, for instance) which has been saturated with a solution of chloride of tin and dried, be moistened with a solution of sugar and exposed to a temperature of 212°, a glistening black spot will be produced at the point touched by the saccharine solution.

Fermentation test.

(87.) The products of the fermentation of sugar serve as a test for its recognition; if we wish to determine its amount, the carbonic acid that is evolved must be collected in a graduated jar over mercury.* When no yeast has been added, the formation of the *Torula cerevisiæ* (see *Pl. V. fig.* 1.) affords a characteristic indication of vinous fermentation: it must, however, be remembered that very similar cellular formations sometimes present themselves in normal urine that has stood for some time (especially in the summer), and hence the presence of this fungus in urine must not be hastily accepted as a proof that it is diabetic.

Its occurrence.

(88.) Sugar (and in the following pages we shall use the simple term sugar in place of glycose or grape-sugar) is a substance of very considerable physiological importance. We shall, therefore, notice somewhat fully the different positions in which it has been found.

Sugar is always found in the *primæ viæ*, especially in the small intestine after the use of saccharine or amylaceous food.

* The yeast employed for the excitement of the fermentation should always be well washed, as it is apt to contain saccharine matter.

Its quantity, however, is generally small, partly because the conversion of starch into sugar is effected slowly, and partly because the sugar is absorbed almost as soon as it is formed.

It may be detected in small quantity in the chyle during the digestion of amylaceous food.*

Until recently it was believed that sugar did not exist in normal blood. Although Magendie † detected it in considerable quantity (in association with dextrine) in the blood of a dog that had been fed for several days upon boiled potatoes, it is to C. Schmidt ‡ that we are indebted for the discovery of the fact that sugar is a normal constituent of the blood of the ox, the dog, the cat, and man. § It was very soon afterwards discovered (almost simultaneously by Lehmann and Bernard) that while the portal blood contains no sugar, or at most a mere trace, (which is the more surprising since sugar is abundantly found in the intestine and absorbed by the veins,) the blood of the hepatic veins is rich in that constituent. It has been distinctly found by von Becker that highly saccharine food exerts an influence on the amount of sugar in the blood. Thus, for instance, he found that the blood of rabbits which had been fed on carrots yielded 0·336% of sugar, while there was only 0·148% in the blood of those animals when fed upon oats, and only 0·097% in their blood

* According to Bernard, the lacteals cannot take up sugar from the intestinal walls, this being solely effected by the blood-vessels. Hence, as a general rule, the chyle cannot contain this substance. The only point at which it can be detected is just before the duct opens into the subclavian vein, when it has received the contents of the lymphatics of the liver, which are always saccharine, both in herbivorous and carnivorous animals.—See his "Leçons de Physiologie," &c., 1855, pp. 311—314.

† Compt. rend. vol. xxx. p. 191.

‡ Charakteristik der Cholera, 1850, pp. 161—163.

§ Schmidt ascertained the quantity of sugar by the carbonic acid yielded on fermentation. In two experiments on ox-blood, the quantities were 0·00069 and 0·00074%; in the blood of a dog it amounted to 0·0015, and in that of a cat to 0·0021%. The blood of two healthy men, one cholera patient, two persons with dropsy, and one with pleurisy, in all cases gave indications of the presence of more or less sugar.

when they had fasted twenty-six hours. Further details on this subject are given in the chapter on "The Blood."

In healthy urine we find no sugar; it only occurs in this fluid under normal relations when very large quantities of sugar have been swallowed at once or in short intervals. It appears, from the experiments of von Becker, that (in rabbits) sugar cannot be detected in the urine unless the blood contain about 0·5% of that substance; if less be present, it appears to be consumed in the circulating fluid.

In diabetes mellitus a very considerable quantity of sugar is daily discharged with the urine. It is occasionally found in the urine in other diseases, as gout, carbuncle, &c.

Bernard has shown that artificial diabetes may be induced by puncturing the floor of the fourth ventricle, sugar appearing in the urine for several hours after the operation.

The same physiologist* has found sugar in considerable quantity in the fœtal urine and in the fluid contents of the amnion and allantois, during the earlier period of intra-uterine life, in the cow and the sheep; it disappears, however, shortly before birth, when these fluids become thick and viscid Dr. W. D. Moore† has sought, unsuccessfully, for sugar in the urine of the human fœtus; as, however, the specimens of urine which he examined were apparently those of the mature fœtus, his failure does not invalidate Bernard's statement.

Sugar in small quantity is invariably found both in the white and in the yolk of eggs; and the amount seems to increase during incubation.

Sugar is always‡ found in the tissue of the liver, even

* Compt. rend. vol. xxx. p. 317. See also his "Leçons de Physiologie Experimentale," 1855, p. 393.

† Experiments as to the Existence of Sugar in the Urine of the Fœtus. —Reprinted from the "Dublin Medical Journal" for 1855.

‡ Bernard gives a long list of the mammals, birds, reptiles, fishes (both osseous and cartilaginous), molluscs, and articulate animals, in whose liver he has found sugar, in his "Leçons de Physiologie Experimentale," 1855, pp. 62, 63.

when no amylaceous or saccharine food has been taken, as in the case of carnivorous animals. The amount of sugar in the liver of man, mammals, and birds is much more considerable than in that of reptiles, fishes, and molluscs, being about 1·5 or 2% in the former classes, and never more than 1% in the latter. In slow wasting diseases, as, for instance, phthisis pulmonalis, the liver is often found to contain no sugar. It appears, from Bernard's researches, that it is not until about the middle of intra-uterine life that the liver contains sugar; previously to that time the muscles (both voluntary and involuntary) and the pulmonary tissue contain it, and it gradually disappears from them as it appears in the liver.

In diabetes sugar occurs in all the serous fluids, in the saliva, in vomited matters, in the solid excrements, and sometimes (but rarely) in the sweat. Bernard mentions the brain, spinal cord, pancreas, and spleen as the only organs in which he failed to detect sugar, in a case of diabetes which he carefully examined during and after death.

Its origin.

(89.) The sugar which is found in the organism originates from two distinct sources. 1. The amylaceous matters of the food are converted into sugar by the saliva, pancreatic fluid, and intestinal juice. 2. Sugar is formed in the liver, most probably from nitrogenous matters — a view which is supported, in the first place, by the abundance in which sugar exists in that structure; secondly, by the fact that the portal blood flowing to the liver is extremely poor in sugar, while the blood of the hepatic veins proceeding from the liver is richer in sugar than the blood of any other vessels; and, thirdly, by a beautiful chemical experiment of Lehmann's*, who has obtained from pure hæmatin (a nitrogenous substance) a saccharine body which reduces oxide of copper, and with yeast resolves itself into carbonic acid and alcohol.

* Bernard's "Leçons," &c. 1855, p. 390.

Since the publication of his "Leçons," Bernard has been led to believe that the sugar is actually formed from the tissue of the liver itself, and not from the blood.*

The physiological importance of sugar will be fully noticed in the chapter on "The Metamorphosis of Tissue."

Sugar of milk.

(90.) *Sugar of milk* crystallises in white, glistening, four-sided prisms with pointed ends, is hard, craunches between the teeth, and is less sweet and less soluble than the other varieties of sugar. It behaves with sulphate of copper and potash in the same manner as glycose. It may be distinguished from glycose, which is the only substance with which it is likely to be confounded, by its crystalline form, by its almost entire insolubility in absolute alcohol, and by the difficulty with which it can be made to ferment. (It seems to be incapable of undergoing fermentation till it has been converted into grape-sugar.)

Its occurrence.

This substance appears to be an integral constituent of the milk of all animals; it is, however, far less abundant in the milk of carnivorous than in that of herbivorous animals. The quantities in which it occurs in the milk of different animals are given in the chapter on "The Milk." There is no very certain evidence of its existence in any fluid except milk: Guillot and Leblanc believe, however, that they have detected it in the blood of milch-cows; and, in a few cases, it has been supposed to have been found in the urine of women shortly after delivery. †

As the milk is the only fluid in which this substance has as yet been found as a regular and normal constituent, we are

* See my review of his book in the "British and Foreign Medico-Chirurgical Review," 1857, vol. xix. p. 41.

† The most satisfactory case is that recorded by Bernard in his "Leçons," &c., p. 427. Sugar, which was apparently glycose from the readiness with which it entered into fermentation, has also been once noticed under similar circumstances by Lehmann. M. Blot, in a memoir published since the above paragraph was written, maintains that sugar invariably occurs in the urine in the puerperal state, and during lactation, and in about half the cases of pregnancy.—Compt. rend., 1856, vol. xliii. p. 676.

led to infer that it is formed in the mammary glands from the glycose contained in the blood.

The use of sugar in the nutrition of the young mammal is noticed in the chapter on "The Metamorphosis of Tissue."

Inosite.

(91.) *Inosite*, or *muscle-sugar*, crystallises with four atoms of water in colourless, four-sided prisms, which part with their water at 212°, have a sweet taste, dissolve readily in water, slightly in strong spirit, and are insoluble in absolute alcohol and ether. It does not reduce oxide of copper, nor is it capable of vinous fermentation; but in the presence of casein or flesh, it undergoes the lactic and butyric fermentation. Scherer, its discoverer, finds that in its anhydrous state it is perfectly isomeric with anhydrous glycose. The following characteristic reaction seems to distinguish it from other sugars and carbo-hydrates. If we evaporate a solution of inosite with a little nitric acid on a platinum spatula almost to dryness, moisten the residue with ammonia and a little chloride of calcium, and then carefully evaporate to dryness, a vivid rose-red tint is developed even if 1-130th of a grain of inosite be present.

Its occurrence.

Inosite was originally found in the juice of the muscular tissue of the heart. Solocoff, who has repeated Scherer's mode of procedure, readily obtained it from this source, but could not procure a trace of it from the juice of any other muscle; and Panum, of Copenhagen, arrived at precisely similar results.

Städeler and Cloetta, in their recent investigations into the chemistry of the glandular structures, have found it in the lungs, liver, spleen, and kidneys. (From 13 pounds of renal tissue 90 grains of inosite were obtained.) They could not detect it in the normal urine either of man or the cow, but obtained unquestionable evidence of its presence in the urine in a case of Bright's disease. Gorup-Besanez was, however, unable to detect it in his examination of the glandular structures.

Nothing is known of its uses; Heintz seems to think it not improbable that it may be formed in the process employed for its extraction.

(92.) *Paramylon* is a glistening white granular starch-like matter, which has been obtained by Gottlieb from the bodies of an infusorium, the Euglena viridis. It is of no general interest. Paramylon.

*Cellulose*, in a state of purity forms a spongy mass, insoluble in water, alcohol, and ether, and in dilute acids and alkalies. It is coloured blue by iodine. Cellulose.

This substance not only forms the basis of all vegetable cells, but is likewise found in some of the lower animals, as, for instance, in the mantle of Phallusia mammillaris, in the tunics of the simple Ascidians, in the leathery mantle of the Cynthiæ, and in the outer tube of the Salpæ. Cellulose, or a substance closely allied to it, has recently been found in the brain and spinal cord of man and the higher animals, as well as in certain morbid deposits.*

(93.) TABULAR VIEW OF THE COMPOSITION OF THE NEUTRAL NON-NITROGENOUS BODIES.

| *Glycerine*, $C_6H_7O_5 . HO$. | | *Cholesterin*, $C_{28}H_{24}O$. | |
|---|---|---|---|
| Carbon . . . | 39·130 | Carbon . . | 84·00 |
| Hydrogen . . | 7·609 | Hydrogen . . | 12·00 |
| Oxygen . . | 43·478 | Oxygen . | 4·00 |
| Water . . . | 9·783 | | |

| *Glycose*, $C_{12}H_{12}O_{12} . 2HO$. | | *Milk-sugar*, $C_{12}H_{12}O_{12}$. | |
|---|---|---|---|
| Carbon . . . | 36·73 | Carbon . . | 46·00 |
| Hydrogen . . | 6·12 | Hydrogen . . | 6·67 |
| Oxygen . . | 48·98 | Oxygen . . | 53·33 |
| Water . . . | 8·17 | | |

* On this subject the reader may be referred to an article by Dr. Arlidge, "On Cellulose, as an Animal Constituent," in the British and Foreign Medico-Chirurgical Review, 1854, vol. xiv. p. 439.

# CHAPTER VI.

## ANIMAL PIGMENTS OR COLOURING MATTERS.

Animal pigments.

(94.) Our knowledge of these substances is very imperfect and unsatisfactory, and they will, consequently, be discussed in a brief manner. We have no means of classifying them according to their rational or even their empirical formulæ, because, with one exception, their formulæ have not been determined. For convenience we shall arrange them as follows: —

1. The blood-pigment — Hæmatin.
2. The bile-pigment.
3. The urine-pigment.
4. Other animal pigments.

Hæmatin.

(95.) *Hæmatin*, whose formula, as determined by Mulder, is $C_{44}H_{22}N_3O_6Fe$, is a dark brown, slightly lustrous matter, devoid of taste and smell, and insoluble in water, alcohol, and ether; it dissolves, however, readily in spirit containing sulphuric or hydrochloric acid, forming a brown solution which, on saturation with an alkali, assumes a blood-red colour; and it is likewise soluble in dilute aqueous solutions of the alkalies and their carbonates. These properties, however, are those of its coagulated (and modified) condition — the only state in which we are acquainted with it, since we have not yet succeeded in separating it in its soluble form from the hæmato-crystallin with which it is associated in the blood-cells.

It is naturally to be expected that the ratio of the hæmatin to the whole mass of the blood should vary with the number

of the blood-corpuscles; and it is probable that the ratio of this pigment to the hæmato-crystallin with which it is combined in the blood-cells is also variable; for the intensity of colour of the individual corpuscles is seen to be very different, when they are viewed through the microscope; and, if we may take the iron as a measure of the hæmatin, equal given weights (say 1000 grains) of hæmato-crystallin or of dried blood-corpuscles usually yield slightly different quantities of iron.

Nothing is known regarding the origin of the blood-pigment.

Its function.

It can hardly be doubted that the hæmatin has a special function to perform in reference to the corpuscles; but we have no certain knowledge on this point. The facts originally established by Bruch, that blood diluted with water to such an extent that the corpuscles become perfectly invisible and are more or less destroyed, becomes of a brighter red when a current of oxygen is passed through it, and is rendered darker by carbonic acid, seem to indicate that the absorption of oxygen by the blood is due (at least in part) to its chemical action on the hæmatin; and Harley's* observations are even more decisive. He took a small quantity of pure hæmatin and put it into a vessel along with 1000 volumes of ordinary air. After the air had been kept in contact with the hæmatin for some months the gas was found to contain — oxygen 16·01 (in place of 20·96), carbonic acid 3·80 (in place of 0·002), and nitrogen 80·19. "The pure colouring principle of the blood, therefore, by exposure to ordinary air, gives off carbonic acid gas, and becomes oxidised in two ways; first, by a loss of carbon, and, secondly, by direct combination with oxygen."

Scherer has obtained from the expressed juice of the spleen an albuminous pigment rich in iron, closely allied in its composition to hæmatin; hence we may infer that the hæmatin

* Proceedings of the Royal Society, for April 17th, 1856, vol. viii. p. 82.

(like the blood-corpuscles) undergoes disintegration in this organ.

Hæmatoidin.

(96.) In old extravasations of blood into the connective tissue, or into the parenchyma of an organ, we often find a crystalline substance, usually of a ruby colour; this has received the name of *hæmatoidin**, and appears to be a modification of hæmatin.

Bile-pigment.

(97.) *Bile-pigment* has never been submitted to a thorough chemical examination, partly because we can only obtain it in very small quantity, and partly because it is so unstable that it not only undergoes various modifications in the animal organism, but it is at once changed by the simplest chemical treatment. Hence we cannot give even an empirical formula to represent its composition. In man and the higher mammals it is originally a brown pigment, but it rapidly becomes greenish brown, and finally green, by oxidation. It is the *cholepyrrhin* of Berzelius, and the *biliphœin* of Simon. It may be obtained as a reddish-brown non-crystalline powder, devoid of taste or smell. It is insoluble in water, but dissolves in alkalies and in alcohol. On the addition of nitric acid to the yellowish brown solution of this pigment a green tint is developed, which soon becomes violet, then red; and, after a considerable period, the red again passes into a yellow: the reaction is best seen when the test contains a little nitrous acid. This brown pigment forms insoluble compounds with the alkaline earths.

Occurrence of bile-pigment.

Bile-pigment usually occurs in fresh bile in a state of solution; but sometimes it is found in the form of granules in a state of suspension. It almost always forms the nucleus and sometimes the whole substance of gall-stones.

* For a full account of hæmatoidin, I must refer to Robin and Verdeil's "Traité de Chimie Anatomique et Physiologique," 1853, vol. iii. pp. 430—437. It has recently been analysed (for the first time) by Robin, who assigns to it the formula $C_{14}H_9NO_3$, and believes that it is formed from hæmatin by the abstraction of the iron and of water. — See Compt. rend. 1855. vol. xli. p. 506.

The bile-pigment which is mixed with the intestinal contents rapidly undergoes oxidation, and passes into a yellow pigment. It is in this state that it occurs in the excrements, unless when diarrhœa is present, in which case the unchanged pigment is found.

Scherer* often detected traces of it in the urine of healthy persons, especially in hot weather.

In cases of icterus it occurs in the blood, the fluids of the eye, the fluid in the subcutaneous connective tissue, &c., and sometimes even in the saliva and the sweat. In this disease it is constantly found in the urine, which is then coloured brownish red, but becomes green by its own acid fermentation, or by the addition of acids.

Its origin.

Although we have no certain evidence regarding the origin of bile-pigment, there are good reasons for believing that it is formed in the liver from the colouring matter of the blood; and this view is much strengthened by recent observations, which show that certain crystals, to which Virchow has given the name of bilifulvin, and which are found in bile that has been long retained in the system, are actually convertible into hæmatoidin.† Frerichs and Städeler‡ have, however, recently (1856) maintained that the bile-pigment is formed from the metamorphosis of the biliary acids. They were first led to this view by the consideration of the fact, established by Lehmann and others, that in those cases in which there is much bile-pigment in the urine there are no traces of the biliary acids in that excretion; while, on the other hand, the biliary acids are often present in considerable quantity when there is little pigment in the urine. Hence they inferred that there must be an intimate relation between the acids and the pigment, and that when the flow of bile was from any cause impeded, the acids either passed unchanged into the urine, or pre-

* Ann. d. Ch. u. Pharm. vol. lvii. p. 133.

† Established by the investigations of Zenker and Funke. See Lehmann's "Physiological Chemistry," 1854, vol. iii. p. 472.

‡ Müller's Archiv, 1856, pp. 55—61.

viously underwent a change into pigment, either in the blood or some other part of the system. Their chemical experiments, which are still in the course of progress, are strongly confirmatory of the accuracy of their views. On treating pure glycocholate and taurocholate of soda with concentrated sulphuric acid, pigments were developed which reacted with nitric acid in precisely the same manner as the bile-pigment.

We know nothing regarding the uses of the bile-pigment. It may have some special part to play in intestinal digestion, but it is more probably a mere product of excretion.

Urine-pigment.

(98.) *Urine-pigment*, like bile-pigment, presents great obstacles to a searching chemical investigation, from the small quantity in which it occurs, and from its instability. It presents various modifications, as is obvious from the numerous tints which different specimens of urine (both normal and morbid) present. Scherer has shown that, when the functions of the lungs, skin, and liver are disturbed, the urine-pigment becomes much richer than usual in carbon. Harley has recently succeeded in isolating what he regards as the essential normal urine-pigment. He terms it *urohæmatin*, and feels convinced, from its always containing iron, and on other grounds, that it is modified hæmatin.

Indigo.

A brilliant blue pigment, similar to and apparently identical with indigo, is sometimes precipitated from the urine; when dried, it glistens like copper, and it dissolves in alcohol, forming a beautiful blue solution. The colour is sometimes not developed except on the addition of a little hydrochloric or nitric acid. It is in cases of Bright's disease that this pigment is most frequently observed. As neither physiology nor pathology has as yet profited much by these investigations, I deem it sufficient to give, in a foot-note*, the re-

* Simon's "Animal Chemistry," vol. ii. p. 328; Heller "On Uroxanthin, Uroglaucin, and Urrhodin," in his Arch. f. Chem. u. Mikrosk. 1845, p. 161; 1846, pp. 19 and 536; and 1852, p. 121; Kletzinsky, on the same subject, in the Arch. f. Chem. u. Mikrosk. 1853, p. 414; Scherer, "On the Formation of Indigo in the Human Organism," in the Ann. d. Ch. u. Pharm. 1854, vol. xc.

ferences to some of the most important memoirs and communications on this subject.

(99.) Of the *other animal pigments*, the most important is *melanin*, which occurs in hexahedral cells in the choroid coat of the eye. It has been submitted both to qualitative and quantitative analysis by Scherer. Like the other pigments, it is most probably a product of the transformation of hæmatin. Its physical importance in the eye is obvious. Melanin.

The black pigment, closely resembling melanin, and occurring in the bronchial glands, and in the pulmonary tissue of aged persons and of colliers, is not chemically identical with it, as is obvious from the analyses of Schmidt* and of Heintz.†

Nothing is known regarding the chemical constitution of the colouring matter of the skin in the dark races.

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(99 *bis.*) TABULAR VIEW OF THE COMPOSITION OF THE ANIMAL PIGMENTS.

| *Hæmatin,* $C_{44}H_{22}N_3O_6Fe$. | | *Hæmatin freed from Iron,* $C_{44}H_{22}N_3O_6$. | |
|---|---|---|---|
| Carbon | 65·35 | Carbon | 70·21 |
| Hydrogen | 5·44 | Hydrogen | 5·85 |
| Nitrogen | 10·40 | Nitrogen | 11·17 |
| Oxygen | 11·88 | Oxygen | 12·77 |
| Iron | 6·93 | | |

p. 120 ; and Dr. Hassall's Memoir "On the presence of Indigo in Human Urine," in the Proceedings of the Royal Society, vol. vi. p. 327, and Philosophical Transactions for 1854, p. 297.

For further information on the urine-pigment generally, I may refer to Heintz, op. cit. pp. 804—810 ; Robin and Verdeil, op. cit. vol. iii. pp. 396—400 ; and Neubauer and Vogel's "Anleitung zur Analyse des Harns," 2nd ed. 1856, pp. 16—20.

* Quoted by Vogel in his "Pathological Anatomy of the Human Body," London, 1847, p. 192. The whole question of the formation of morbid pigments is admirably discussed in this volume.

† Zoochemie, 1853, p. 812.

*Cholepyrrhin or Biliphœin,*
$C_{32}H_{18}N_2O_9$
(according to Heintz).

| | |
|---|---|
| Carbon . . . | 60·88 |
| Hydrogen . . | 6·05 |
| Nitrogen . . | 9·12 |
| Oxygen . . . | 23·95 |

*Brown Urine-pigment*
(Scherer).

| | |
|---|---|
| Carbon . . . | 61·37 |
| Hydrogen . . | 6·19 |
| Nitrogen . . | 7·03 |
| Oxygen . . . | 25·41 |

*Pigment of Choroid Coat*
(Scherer).

| | |
|---|---|
| Carbon . . . | 57·54 |
| Hydrogen . . | 5·98 |
| Nitrogen . . | 13·77 |
| Oxygen . . . | 22·71 |

*Pigment from Melanotic Tumour*
(Heintz).

| | |
|---|---|
| Carbon . . . | 53·44 |
| Hydrogen . . | 4·02 |
| Nitrogen . . | 7·10 |
| Oxygen . . . | 35·44 |

# CHAPTER VII.

## THE PROTEIN-BODIES.

(100.) Under this title we include the following substances: — Protein-bodies.

Albumen.
Fibrin.
Syntonin or Muscle-fibrin.
Casein.
Globulin.
Hæmato-crystallin.

Albumen, fibrin, and casein are common both to the animal and vegetable kingdoms. In the present volume these substances are, however, considered solely in reference to their occurrence in the animal organism.

These substances differ so slightly from one another in their ultimate composition, in many of their properties, and in the products of their decomposition, that it is not surprising that the idea should have suggested itself that they possessed a common radical.

Mulder believed that he had discovered this radical, which, from its importance, he designated as *Protein* (from *πρωτέυω*, I hold the first place, or am first); while he regarded albumen, fibrin, casein, &c. (which at that period, 1838, were termed *albuminous bodies*), as combinations of this protein with sulphur and phosphorus, or simply with sulphur. According to Mulder, the true composition of protein is (in 100 parts) 54·7 of carbon, 6·8 of hydrogen, 14·2 of nitrogen, and 24·3 of oxygen; and its formula is $C_{36}H_{25}N_4O_{10} + 2HO$. Protein.

Although great doubt has recently been thrown on Mulder's

protein-theory*, we have retained the name of protein-bodies or protein-compounds as being the most convenient for designating this group of substances.

General characters of the protein-bodies.

The protein-bodies may be generally described as nearly colourless, neutral, nitrogenous bodies, soluble in potash-solution, and not yielding gelatin when boiled with water. They all present two modifications differing essentially from one another, in one of which they are soluble, and in the other nearly or quite insoluble. They exist in the animal organism only in the soluble modification, even when they are not dissolved and cannot be dissolved in water. Most of them are transformed into the insoluble state by boiling, by the mineral acids, and by numerous salts; one of them, fibrin, undergoes this modification on simple removal from the animal organism. This passage from the soluble into the insoluble form is termed coagulation, but we do not clearly know what chemical change takes place in the process. "It might be supposed (says Lehmann†) that coagulation depended solely on a rearrangement of the molecules, similar to that which is observed when oxide of tin, titanic acid, &c. assume the insoluble state under the influence of heat; but direct observations have shown that in the coagulation of the protein-bodies something is removed from them by solution, although this may not amount to more than 2% of the original substance: it may be regarded as an established fact that, in the coagulation of albumen, alkali is separated from the soluble modification, while in that of hæmato-crystallin there is a separation of an acid and salts. Hence we must regard the soluble modifications as compounds which, on heating, lose a proximate constituent, while the remainder (forming the chief mass) becomes insoluble; the latter, however, at the same time loses the power of again uniting itself directly with the

* See Lehmann's "Physiological Chemistry," vol. i. pp. 328—9.

† Handbuch der Physiologischen Chemie, 1854, p. 74.

separated substance, as is also the case generally with conjugated substances."

Properties of the soluble protein-bodies.

The *soluble protein-bodies* in their dried state form pale yellow, transparent, pulverisable masses, devoid of smell or taste, which are soluble in water, but insoluble in alcohol and ether. They are precipitated from their watery solutions by alcohol, by the mineral acids, and by tannic acid, but not by the other vegetable acids, or by the alkalies: most mineral salts cause precipitates, and the precipitate generally contains combinations both of the acid and of the base with the protein-body. One of their most characteristic properties is, that they are precipitated neither by acetic acid nor by the neutral alkali-salts, but that when the two are simultaneously added, they are thrown down: the precipitate which is thus formed differs in its properties from the original substance, but is soluble in water—a fact which shows that it is not reduced to the coagulated form.

Of the insoluble protein-bodies.

The *insoluble protein-bodies*, when freshly precipitated, are of a white colour, in flakes or small clots, or viscid and glue-like; when dried they may be reduced to a whitish powder. They dissolve in concentrated acetic acid, and other organic acids, as well as in the ordinary (tribasic) phosphoric acid, and they are precipitated from these acid solutions both by the yellow and the red prussiate of potash. With moderately concentrated mineral acids they enter into combinations which present the peculiarity of being insoluble in acidulated water, but soluble in pure water. When heated with concentrated nitric acid they assume an intense lemon-yellow colour; while concentrated hydrochloric acid, with the aid of gentle warmth and prolonged exposure to the air, gradually induces an intense blue tint, and partially dissolves them into a blue fluid.

Millon's test.

The most delicate test for the protein-bodies, whether they are dissolved in a fluid or simply interspersed in a tissue, is afforded by the application of a solution of mercury, prepared

by dissolving one part of mercury in two of nitric acid of specific gravity 1·41. On the addition of this solution, and on raising the temperature to from 140° to 212°, an intense red colour is evolved, which does not disappear either on prolonged boiling or on exposure to the atmosphere. This is known as Millon's test.* It should be mentioned that it gives a similar reaction with the gelatigenous substances which form the subject of the next chapter.

In microscopic examinations of the tissues, a solution of iodine, which developes a deep brownish-yellow colour with these bodies, is employed by Histologists. For this purpose, an aqueous solution of iodine with iodide of potassium is employed.

It has been already mentioned that all the protein-bodies contain sulphur, and some of them phosphorus. Another point worthy of notice is, that they are always accompanied with fats, alkalies, and salts of lime (especially the phosphate, which, according to Mulder, occurs in a definite quantity in albumen, fibrin, and casein, and is doubtless combined with them).

Their products of decomposition.

(101.) The products of the decomposition of these bodies, when acted upon by strong mineral acids, by oxidising agents, and by alkalies, have been fully studied by various German chemists, amongst whom we may especially mention Schlieper and Guckelberger.

When digested for a considerable time with strong sulphuric or hydrochloric acid, they yield leucine, tyrosine, ammonia-salts, and other products that have not yet been fully examined.

Under the action of oxidising agents, such as chromic acid or black oxide of manganese and sulphuric acid, they yield, as non-nitrogenous products, all the acids of the butyric-acid group and their aldehydes, from formic to caproic acid; and,

* Ann. de Chim. et de Phys. 1850, vol. xxix. p. 507.

in addition to these, benzoic acid and hydride of benzoyl (oil of bitter almonds); while the principal nitrogenous products are ammonia and hydrocyanic acid.

When digested for some time with solutions of the caustic fixed alkalies, or when fused with them, there is a development of ammonia, and of both formic and carbonic acids, while various neutral or basic nitrogenous substances are formed, namely, leucine, tyrosine, glycine, &c.

These bodies spontaneously undergo the process of putrefaction—that is to say, without any apparent cöoperation of other matters, and solely by the influence of atmospheric agents. Amongst the products of their putrefaction there are always to be found carbonate, butyrate, and valerianate of ammonia, sulphide of ammonium, leucine, and tyrosine.

Albumen.

(102.) *Albumen*, the great type of the protein-bodies, occurs in very different modifications, which seem to depend on the substances mixed or combined with it; namely, alkalies and salts. Hence the albumen of the blood differs in several points of view from that of the egg, and even these kinds of albumen do not present precisely similar reactions in all cases.

Its characters.

It is doubtful whether the composition of albumen is accurately represented by any formula that has yet been calculated. According to Mulder* an equivalent of albumen is represented by the formula $5(Pr + 2HO) + 2SNH_2$; Pr being $= C_{36}H_{25}N_4O_{10}$ (see p. 101), while Lieberkühn gives the simpler formula $C_{72}H_{56}N_9O_{22}S$.†

Albumen has few marked characters. In his "Handbuch," Lehmann describes it "as that protein-body whose solution perfectly coagulates at 63° (145·4° F.): it must, however, be recollected that the coagulability is in every point of view a thoroughly relative property; for both the degree of tem-

* Mulder's "Chem. Untersuchungen," (translated into German by Voelker,) p. 207.

† See the Tabular View, at the end of this Chapter.

perature requisite to induce this change, and the form in which the albumen coagulates, are mainly dependent on the admixture or combination of other substances with it." On the addition of an excess of alkali, or of a free acid which does not precipitate it (as acetic or ordinary phosphoric acid), it ceases to be coagulated by heat, but it is thrown down in the insoluble form on the subsequent neutralisation of the fluid. Albumen coagulates in somewhat different forms, according to the reaction of the fluid in which it is dissolved. Thus, on the evaporation of a very acid or of a very alkaline solution of albumen, a thick, colourless membrane of coagulated matter forms upon the surface, which, until recently, was regarded as a certain indication of the presence of casein: from faintly alkaline solutions it either coagulates in a gelatinous form, or else in such minute particles as to give the fluid a milky appearance; while from perfectly neutral or faintly acid solutions it coagulates in flakes, which soon sink and leave a clear supernatant fluid.

Tests.

The coagulability of a fluid by heat is usually regarded as evidence that it contains albumen; this, however, is not a sufficient test, since other bodies (shortly to be described) also coagulate when boiled, and, as we have already shown, albumen under some conditions does not coagulate. If the fluid in which we are searching for albumen is either very acid or very alkaline, we must either neutralise it, or treat it with a saturated solution of hydrochlorate of ammonia before heating it. It sometimes happens that on boiling a specimen of urine we obtain a precipitate which closely resembles coagulated albumen, but in reality does not contain a trace of that substance, being composed of earthy phosphates (phosphate of lime and magnesia, and ammoniaco-magnesian phosphate), which, if the fluid be only slightly acid, or neutral, are readily thrown down on boiling: in such cases, however, all doubt may be removed by the addition of a few drops of dilute nitric or hydrochloric acid, which will dissolve

the phosphates but will not affect coagulated albumen. As a general rule, when a fluid coagulates on heating, and is likewise precipitated by the mineral acids, corrosive sublimate, &c., we entertain no doubt of the presence of albumen: but, strictly speaking, we cannot distinguish albumen in some of its modifications with positive certainty from the similar protein-bodies, especially in the coagulated condition.

Its occurrence.

Albumen is always found in the body in a state of solution, and generally (if not always) in combination with a small quantity of alkali. (In some experiments made by Lehmann on the albumen of hens' eggs, he found that 1·58 parts of soda were combined with 100 of albumen.)

Albumen occurs in all those animal fluids which supply the organism with the materials necessary for nutrition and the renovation of effete matters. Hence it is a principal constituent of the blood, lymph, and chyle, of the fluids of the egg, &c.

It is, moreover, always found in transudations (whether normal or abnormal) from the capillaries, as, for instance, in the fluids in the serous cavities; and in the parenchymatous fluids of all organs in which active cell-life is going on, as, for instance, the liver, kidneys, brain, and muscles.

It forms the main solid constituent of the serum of the blood, occurring in the proportion of from 7·9 to 9·8%, and amounting to about 85% of the solid residue. In the blood itself it fluctuates in the normal state between 6·3 and 7·1%.

The secretions, as, for instance, the saliva, gastric juice, bile, and mucus, contain no albumen in their normal state: the pancreatic juice *, however, contains a substance extremely similar to, if not identical with albumen, which coagulates on being heated; and albumen may occur in any of the above-named fluids when their secreting surfaces are inflamed.

* The albuminous substance of the pancreatic juice has been carefully studied by Bernard. See his Memoir, in the Arch. Gén. de Méd. 1848, 4th series, vol. x. p. 68.

Albumen has been detected by several observers in the liquor amnii, and is found to be more abundant in that fluid in the earlier than in the more advanced stages of fœtal existence.

In the normal condition no albumen is contained in the excretions, and its appearance indicates either disease of the excreting organ, or a very abnormal state of the blood. The conditions under which it occurs in the urine and the fæces will be fully noticed when we treat of those substances.

Its origin.

There can be no doubt that the albumen of the animal fluids is derived from the protein-bodies which enter largely into the composition of most articles of food; but we are altogether ignorant of the manner in which casein, fibrin, &c., after their conversion in the stomach into peptones* and their subsequent absorption, are further changed into normal albumen.

Its uses.

The importance of albumen, in connection with the formation and nutrition of the nitrogenous tissues, is sufficiently indicated from the fluids in which it occurs; and, as will be shown in a future page, this substance requires only very slight modifications to be converted into the contractile structure of which the muscles are composed, or into the contents of the nerve tubes. We do not at present distinctly know the exact manner in which cells and tissues are constructed from albumen; but there is reason to believe that albumen is, in the first instance, converted into fibrin.

Fibrin.

(103.) *Fibrin* is distinguished from all the other protein-bodies by its separation in a solid state, in the form of extremely delicate filaments or lamellæ, from any fluid in which it is dissolved, very shortly after the abstraction of the latter from the organism.

Its characters.

Of the properties of dissolved fibrin we know little more

* Peptones are protein-bodies that have been acted upon and modified by the gastric juice. They differ very much in their physical properties from the protein-bodies, from which they are derived, but they resemble one another very much in their solubility in water, their insolubility in alcohol, and their incapacity of coagulating.

than that it is precipitated from its solution by a strong solution of potash (and by ether), but not by acetic acid or ammonia. The spontaneous coagulation of the fibrin in the blood may be greatly retarded by dilute solutions of the alkaline sulphates, nitrates, &c., and may even be entirely prevented by concentrated solutions.

Spontaneously coagulated fibrin differs in several respects from fibrin that has been coagulated by boiling: it absorbs oxygen and undergoes the process of putrefaction more readily than any other protein-body, and it is further distinguished by the fact that in water, containing 0·1% of hydrochloric acid, it swells into a jelly-like mass, but does not dissolve like the other protein-bodies, and that when digested with a dilute solution of nitre (1 part of the salt in 17 parts of water) it dissolves into a fluid coagulable by heat.

Boiled fibrin differs in no essential point from the other coagulated protein-bodies.

Composition.

The ultimate analyses of fibrin, made by different chemists, differ too much to enable us to calculate even an empirical formula for the composition of this substance. In the fibrin of ox-blood Rüling found 1·319, and Verdeil 1·593% of sulphur, while Mulder found only 1·2%; according to the last-named chemist it also contains 0·3% of phosphorus. Most recent analyses tend to show that it contains rather more oxygen than albumen. A little fat, consisting chiefly of ammonia and lime in combination with a fatty acid, is always associated with fibrin, and amounts to about 2·6% of the dried substance. Like all the protein-bodies, it likewise contains phosphate of lime.

The ordinary test for fibrin in solution is its spontaneous coagulability. Coagulated fibrin, such as is supposed to occur in exudations, tubercular deposits, &c., cannot, as a general rule, be distinguished from the other coagulated protein-bodies.

Its occurrence.

Fibrin occurs principally in the blood, the lymph, and the chyle.

In healthy venous blood it hardly ever reaches 0·3%; it generally fluctuates between 0·20 and 0·27%. Small as its amount is, it varies in quantity more than any other constituent of the blood, as in some morbid conditions it exceeds its ordinary average by five or six times. It also varies in normal blood in different vessels; thus arterial blood contains more fibrin than venous blood, the blood of the splenic vein contains very little, and that of the hepatic veins scarcely any fibrin. The blood of infants contains less fibrin than that of adults; and in the latter months of pregnancy there is a considerable augmentation of this constituent.

During an animal diet the amount of fibrin is greater than during a vegetable diet; the quantity of fibrin is moreover increased during prolonged fasting.

The blood of the herbivorous animals contains more fibrin than that of the carnivorous, and the blood of birds even more than that of the herbivorous animals.

A constant and great augmentation of the fibrin occurs in inflammatory diseases, especially in acute articular rheumatism and in pneumonia; in these diseases it has been found to exceed 1%. No diseases are known in which there is a constant diminution of the fibrin.

In the lymph and chyle this constituent occurs in considerably less quantity than in the blood.

In inflammatory exudations we find fibrin in the fluid contents of the serous cavities, or on the mucous membrane (as in croup), or in the parenchyma of organs; in these cases it most commonly occurs in a state of spontaneous coagulation. The fibrin occurring in exudations and transudations occasionally differs essentially, both in its physical and chemical characters, from true blood-fibrin, sometimes closely resembling the syntonin or muscle-fibrin described in the next paragraph.*

* On this subject I may refer to Memoirs by Gorup-Besanez, "On a peculiar Modification of Fibrin," in Ann. d. Ch. u. Pharm. 1855, vol. xciv. p. 166, and by Bödeker, "On the Analysis of a Transudation in the Pleural Cavity," in Zeitsch. f. rat. Med. 1855, vol. vii. p. 142.

From what has been already stated, we feel justified in concluding that fibrin is formed from albumen and not directly from the food. The slight excess of oxygen in fibrin would lead to the inference that it is formed by a process of oxidation. This inference has, however, led to serious error in reference to the increase of fibrin in inflammation; since on the assumption that the fibrin is formed by a process of oxidation, it was very erroneously concluded that the augmentation of this constituent in inflammation is dependent on an increased rapidity of the process of oxidation; and that, consequently, inflammation is nothing more than an actual process of combustion. This hypothesis was for many years unhesitatingly accepted by physicians, without its apparently occurring to them that, even if an excessive supply and absorption of oxygen might, on purely chemical grounds, be regarded as the cause of an increase of fibrin, this explanation was altogether incompatible with the fact that in pneumonia, when a considerable portion of the lungs is rendered impervious to air, a greater quantity of fibrin is found than in almost any other disease. Physiological facts seem to point to exactly the opposite hypothesis, that the augmentation of fibrin in inflammatory blood is caused by an insufficient supply of oxygen. When oxygen is abundantly introduced into the blood, the fibrin rapidly undergoes further transformations; thus we find less of it in children and in healthy adults than in pregnant women and in patients with inflammatory diseases; for in the latter cases the respiration is more or less impeded, and the quantity of oxygen conveyed to the blood is not sufficient to effect the further normal oxidation or transformation of the fibrin, which therefore accumulates in the circulating fluid.

Its origin.

It has long been a disputed question whether fibrin belongs to the progressive or regressive metamorphosis; that is to say, whether it is a factor in the elaboration or in the disintegration of the tissues. For a full discussion of the sub-

Its physiological importance.

ject I must refer to Lehmann's Physiological Chemistry, vol. i. pp. 361-364., and to Simon's Lectures on General Pathology, pp. 50-52. As in the process of acid fermentation there are intermediate stages between the two extremes of alcohol and acetic acid, so in the present case we may regard fibrin as representing one of the stages of oxidation which albumen undergoes in its transition into the more highly oxidised elements of the tissues.

Syntonin, or muscle-fibrin.

(104.) *Syntonin**, or *muscle-fibrin*, forms, while moist, a snow-white coherent, somewhat elastic mass, which may be removed from the filter on which it is collected, in the form of laminæ or membranes. The following are the most characteristic properties by which it may be distinguished from spontaneously coagulated blood-fibrin, or from albumen. It differs from the former by its being soluble in water containing $0{\cdot}1\frac{0}{0}$ of hydrochloric acid, from which it is precipitated in a gelatinous form on the neutralisation of the acid; by its insolubility in nitre-water (6 parts of $KO . NO_5$ to 100 of water); and by its swelling and becoming gelatinous, but not dissolving, in a moderately concentrated solution of carbonate of potash; while it may be readily distinguished from the latter by the fact that it is precipitated from its alkaline solutions by the chlorides of sodium and potassium. That it is not identical with blood-fibrin is also obvious from the results of its ultimate analysis.

We are indebted to Liebig for the discovery that syntonin, which is the most important constituent of the fibrillæ of striated muscle, is chemically distinct from the fibrin of the blood. Lehmann has subsequently shown that it not only exists equally in the voluntary and involuntary (or smooth) muscles, but in all those tissues in which Kölliker's fibre-cells occur; as, for instance, in the middle arterial coat and in the spleen.

The fact that this substance is the principal constituent and

* Derived from *συντείνειν*, to render tense.

the essential basis of all the contractile tissues, seems sufficient to indicate its uses; but how far, or why it is better qualified than the other protein-bodies for the manifestations of vital contractility, we cannot tell.

(105.) *Casein* chiefly differs from the other protein-bodies in its mode of coagulation. Acetic and lactic acids throw down casein from its solutions, the precipitate redissolving in an excess of the acetic acid. Casein is coagulated by the mucous membrane of the fourth stomach of ruminants (rennet) and by the gastric juice of carnivorous animals. It is not precipitated by heat; but if it be boiled with a solution of sulphate of magnesia or of chloride of calcium, it is thrown down in a state of combination with the magnesia or lime, although it is not precipitated by heat; if, however, it be exposed in an open vessel to a high temperature, a white, tough membrane of coagulated casein soon forms on the surface, and, when removed, is soon reproduced. Scherer has shown that it cannot coagulate in this membranous form unless in the presence of oxygen. Casein.

Notwithstanding the above peculiarities of casein, it is by no means easy to distinguish it with certainty from alkaline albuminates or acid solutions of albumen. The following method is recommended by Lehmann for determining whether casein coexists with albumen in a fluid. The fluid must be boiled for some time, a little hydrochlorate of ammonia having been first added in order to remove the albuminate of soda; we then filter, and ascertain whether sulphate of magnesia or chloride of calcium give a precipitate at the ordinary temperature; if this be the case, the precipitate must be removed by filtration before we boil the fluid with the view of finding casein. If a precipitate is now caused by boiling, it must consist of casein in combination with magnesia or lime; and it will be found that in this case rennet will also coagulate the fluid.

Casein has been frequently analysed, but these analyses

have not led to any certain empirical formula, much less to a rational one.*

Its occurrence.

This substance occurs in the milk of all mammals. In human milk it ranges from about 2·7 to more than 3%; in cows' milk it is rather more abundant; and in that of carnivorous animals (the dog) it ranges from 8·3 to 13·6%. In the milk of the ass it does not exceed 1·95%.†

A substance very similar to casein occurs in small quantity in the blood, and has received the name of serum-casein. It seems to be more abundant in the serum of women than in that of men (amounting in the former, according to Panum‡, to 0·3%), and especially so during a certain time after delivery (when it ranges from 0·99 to 1·25%). It is said, also, to exist in excess in placental blood.

It likewise occurs in the interstitial juice of the muscles of organic life (in short, wherever Kölliker's contractile fibre-cells are found), in the expressed juice of the thymus gland and of the connective and elastic tissues, and in the fluid of the allantois.

Casein is, moreover, found in the yelk of egg. Here it occurs in a state of intimate admixture with albumen, and this admixture was until very recently looked upon as a special protein-body, and has been described under the name of *Vitellin.*

Its origin and uses.

Nothing is accurately known regarding the origin of casein; that is to say, we cannot tell whether it is primarily elaborated from other protein-bodies in the blood, or in the mammary glands: neither is it known why albumen—the ordinary nutrient matter—is replaced in the milk by casein; and we are perfectly in the dark as to the functions exercised by casein in the juices of the various tissues.

* See the Tabular View at the end of this Chapter.

† See the Chapter on "The Milk."

‡ Arch. f. Pathol. Anat. vol. iii. pp. 251—272. See also Moleschott, in Arch. f. Physiol. Heilk. vol. xi. pp. 105—111.

(106.) *Globulin*, or *crystallin*, closely resembles albumen; it, however, does not coagulate at a temperature lower than 163°, when its solution either becomes milky or is converted into a globular mass, according to its concentration. The following reaction is characteristic of globulin:—its solution is not precipitated either by acetic acid or by ammonia, but it becomes very turbid when the acid solution is neutralised by ammonia, or the ammoniacal solution by acetic acid. Globulin also presents the peculiarity of being precipitated from its aqueous solution by carbonic acid, the precipitate which is formed being again soluble in water, if the carbonic acid be displaced by the introduction of another gas. Globulin, or crystallin.

Globulin has hitherto only been detected with certainty in the crystalline lens, where it amounts to nearly 36%. Berzelius held the view that this protein-body obtained from the lens was identical with the coagulable matter of the red blood-corpuscles, and hence assigned to the two the common name of globulin—a view which we shall show to be incorrect in the next paragraph: it is sufficient here to state that the protein-body contained in the blood-corpuscles is, under certain conditions, crystallisable, while, under similar conditions, the globulin of the lens cannot be made to assume the crystalline form.

The object of the globulin in the fibres of the lens is too obvious to require any remarks; and it is interesting to observe, that while a refractive fluid is thus produced, the lens itself is at the same time rendered achromatic, not merely by its anatomical structure, but also by its central portion being filled with a concentrated fluid which gradually becomes more diluted towards the capsule.*

(107.) *Hæmatocrystallin* is the only one of the protein- Hæmatocrystallin.

* For the knowledge of this fact we are indebted to Chenevix, who found that the specific gravity of an entire lens was 1·0765, while that of the nucleus was 1·194.

bodies that can be obtained in a crystalline state, and the very forms of the crystals show us that we have to deal with three or four different substances, or distinct modifications of the same substance. This crystalline substance, when obtained from the blood of guinea-pigs, rats, or mice, separates in tetrahedra; that from the blood of man, and most carnivorous animals, in prisms; that from the blood of the squirrel in hexagonal plates; and that from the hamster, in rhombohedra. (*Plate IV. fig.* 4.) These crystals are devoid of smell and taste, and are always of a red colour, but appear of a lighter tint individually, when seen under the microscope. The solubility of the different forms is very different; the prisms (from a dog) dissolving in 90 parts of water, while the tetrahedra require 600 parts. Hæmatocrystallin differs from all the other protein-bodies in not being precipitated from its solutions by nitrate of silver, chloride of mercury (corrosive sublimate), chloride of tin, or basic acetate of lead; it is, however, thrown down by nitrate of suboxide of mercury and bichromate of potash. The solution of the tetrahedral crystals coagulates at 146·4°; that of the other crystals requires two or three additional degrees of temperature: the supernatant fluid then reddens litmus. All these crystals so obstinately retain the blood-pigment that it is impossible to obtain them perfectly free from it.

The hæmatocrystallin obtained from the blood of the dog has been analysed by Lehmann, but its formula has not yet been established.

This chemist has also made the remarkable discovery that this substance may be broken up into a nitrogenous substance (which has not been fully investigated) and a variety of sugar closely corresponding to, if not identical with, glycose. In this manner we may ultimately discover its rational formula.

Hæmatocrystallin occurs only in the red blood-corpuscles.

It seems to be present in all the vertebrated animals. We know nothing of its origin.

Its uses are described in the chapter on "The Blood." See § 197.

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TABULAR VIEW OF THE ULTIMATE COMPOSITION OF THE PROTEIN-BODIES.

*Protein*, $C_{36}H_{25}N_4O_{10}$.

| | |
|---|---|
| Carbon | 57·29 |
| Hydrogen | 6·63 |
| Nitrogen | 14·86 |
| Oxygen | 21·22 |

*Albumen* (*according to Mulder's formula*).*

| | |
|---|---|
| Carbon | 52·97 |
| Hydrogen | 6·81 |
| Nitrogen | 15·11 |
| Oxygen | 23·54 |
| Sulphur | 1·57 |

*Do.* (*according to Lieberkühn's formula*).

| | |
|---|---|
| Carbon | 53·59 |
| Hydrogen | 6·95 |
| Nitrogen | 15·63 |
| Oxygen | 21·84 |
| Sulphur | 1·99 |

*Blood-fibrin* (*analysed by Mulder*).

| | |
|---|---|
| Carbon | 52·7 |
| Hydrogen | 6·9 |
| Nitrogen | 15·4 |
| Oxygen | 23·5 |
| Sulphur | 1·2 |
| Phosphorus | 0·3 |

*Muscle-fibrin* (*analysed by Strecker*).

| | |
|---|---|
| Carbon | 55·23 |
| Hydrogen | 7·39 |
| Nitrogen | 15·84 |
| Oxygen | 20·33 |
| Sulphur | 1·21 |

* In this formula, Mulder neglects the phosphorus, which, according to his analysis, amounts to 0·4%. According to Lieberkühn, pure albumen contains no phosphorus.

*Casein* (*analysed by Völcker*).

| | |
|---|---|
| Carbon . . . | 53·61 |
| Hydrogen . . . | 7·14 |
| Nitrogen . . . | 15·47 |
| Oxygen . . . | 17·99 |
| Sulphur . . . | 1·11 |
| Phosphorus . . | ·74 |

*Hæmatocrystallin from dog's blood* (*mean of three analyses by Lehmann*).

| | |
|---|---|
| Carbon . . . | 55·28 |
| Hydrogen . . | 7·11 |
| Nitrogen . . . | 17·33 |
| Oxygen . . . | 20·05 |
| Sulphur . . . | 0·23 |

# CHAPTER VIII.

## PROXIMATE DERIVATIVES OF THE PROTEIN-BODIES.

(108.) THE substances belonging to this group differ very much from one another in their physical and their chemical properties; almost their sole points of correspondence being that they only occur in the animal body, where they form the bases of certain tissues, that they are neutral, insoluble in cold water, and that they all contain nitrogen. In their behaviour towards acetic acid and ferrocyanide of potassium, and towards strong hydrochloric and nitric acids, they exhibit none of the essential characteristics of the protein-bodies. Their general properties.

The following are the only substances of this group which have hitherto been submitted to an accurate chemical examination: —

Glutin-yielding substance, or ossein;
Chondrin-yielding substance;
Elasticin, or the substance of elastic tissue;
Fibroin; and
Chitin.

(109.) The term *ossein* was first applied by Robin and Verdeil, and subsequently by Fremy*, to the substance in the osseous tissue which yields glutin. It is obtained by the prolonged action of dilute hydrochloric acid on bone, which must be subsequently washed repeatedly with water, and treated with alcohol and ether. It is insoluble in water, Ossein.

* In his "Recherches Chimiques sur les Os." Ann. de Chim. et de Phys. 1855. vol. xliii. p. 51.

but is converted into glutin (one of the forms of gelatin) by the action of boiling water — a transformation which is very much facilitated if a little acid be present. The ossein yielded by different kinds of animals requires different times for its conversion into glutin, and the ossein of young animals changes more rapidly than that of adults of the same species. Fremy's analyses show that ossein is isomeric with the glutin which it yields: moreover, the amount of glutin is precisely the same as that of the ossein that yields it. It appears to exist in the bones in a state of freedom; that is to say, not in combination with any of the salts of lime.

Glutin.

*Glutin*, when in a pure state, is colourless, transparent, of a horny appearance, brittle, heavier than water, and devoid of smell and taste; it is especially characterised by its solubility in hot water, from which it gelatinises on cooling. It is precipitated from its hot watery solution by chlorine, chloride of mercury (corrosive sublimate), bichloride of platinum, tannic acid, and alcohol. On dry distillation, it yields large quantities of the volatile alkaloids Petinine ($C_8H_{11}N$) and Picoline ($C_{12}H_7N$), together with carbonate of ammonia: with chromic acid it yields the same products of decomposition as the protein-bodies, but a much larger quantity of valerianic acid: with alkalies, it yields an abundance of leucine and glycine.

We are unable to assign, with any degree of certainty, a chemical formula to glutin. Its ultimate composition is given at the end of this chapter; but since this analysis was made, it has been found to contain from 0·12 to 0·14% of sulphur.

Glutin may be obtained, by mere boiling, from various tissues; not only from bone-cartilage (after its ossification), but from the tendons, the skin, the bladder, &c.

Its physiological relations.

As far as we yet know, glutin only normally occurs preformed in the juice of the spleen (Scherer); it is sometimes found in the blood in the diseased condition known as

leucæmia (see § 221), and is an occasional constituent of pus (Spiess, Weismann), and of the expressed juice of carcinomatous tumours (Schirmer and Wimmer).

Since cartilage and connective tissue yield, when submitted to ultimate analysis, precisely the same results as the glutin that can be obtained from them, it is probable that one is convertible into the other by a mere re-arrangement of the atoms.

It is remarkable that the embryo, as long as it remains in the egg, contains no gelatigenous tissue (Hoppe).

We know nothing of the conditions under which the substance which yields glutin is formed from the protein-bodies; that there are intermediate or transition stages between the two, is borne out by Scherer's observation that leucæmic blood sometimes contains, not only glutin, but a substance which, in its chemical relations, stands between it and the protein-bodies.

It is very evident that those tissues of the animal body which yield gelatin rank low in the scale of organisation, and that their uses are almost entirely of a physical character: thus they form strong points of connection for muscles (the tendons), they moderate shocks or concussions by their elasticity (the cartilages of bone), they protect the body from rapid changes of temperature by their bad conducting power (the skin), and they are of service through their transparency (the cornea).

Chondrin.

(110.) The substance which yields chondrin, that is to say, the organic matter contained in the permanent and articular cartilages and the fibro-cartilages, as well as bone-cartilage before ossification, has never yet been carefully examined. Hence we must confine our remarks to *chondrin* itself, the variety of gelatin that is yielded by these substances in the same manner that bone yields glutin. Chondrin closely resembles glutin in its physical characters, except that it is usually more coloured, and swells to a greater extent (to 11

or 12 times its original size) in cold water. It differs from glutin in being precipitated by hydrochloric acid, acetic acid, acetate of lead, alum, and sulphate of peroxide of iron, as well as by the reagents mentioned as throwing down gelatin. When treated with strong sulphuric acid it yields leucine, but no glycine; but when treated with a concentrated solution of potash, or fused with hydrated potash, it yields leucine, glycine, and other products of decomposition, amongst which, however, Hoppe, who has carefully studied this substance, could not detect tyrosine. When oxidised with chromic acid, it developes much hydrocyanic acid, but no formic or acetic acid.

Chondrin has been analysed by Mulder and by Scherer, and the results of the former are given in the Tabular View at the end of this chapter. In addition to the four ordinary elements, Mulder found 0·38% of sulphur, and about 4% of phosphate of lime which seemed to be chemically combined with the other elements.

Bone-cartilage before ossification yields chondrin; and the same is the case in various diseases of the osseous tissue. Hence chondrin and glutin must stand in a definite relation to one another, although we do not yet know what that relation is.

In his recent memoir on the chemistry of pus, Bödeker states that chondrin occasionally occurs in that fluid.

The uses of the chondrin-yielding substances are much the same as those of the substances yielding glutin.

Elasticin.

(111.) *Elasticin*, or the substance of elastic tissue, is insoluble in all known menstrua: it requires thirty hours' boiling in a Papin's digester at a temperature of 320° to reduce it to a brown fluid, which does not gelatinise on cooling. With strong sulphuric acid, it yields leucine, but no glycine.

It occurs in connective tissue (in the form of nuclear fibres), and is most abundant in the true elastic tissue, as, for in-

stance, in the ligamentum nuchæ, the ligamenta subflava, the inferior vocal chords, and the middle arterial coat.

Its uses are of a purely physical character.

(112.) *Fibroin* has hitherto been obtained only from silk and gossamer threads, and is consequently a substance of little general interest. A similar substance has been obtained from sponge. Fibroin.

(113.) *Chitin* is a white amorphous substance, which generally retains the form of the tissue from which it is derived. It is insoluble in water, acetic acid, and alkalies, but dissolves with decomposition in the strong mineral acids. It presents two peculiarities when submitted to dry distillation:—it does not fuse, but leaves a carbonaceous mass which, on microscopic investigation, always exhibits the form of the original tissue; and further, notwithstanding it contains nitrogen, it yields acid products of distillation, from which it may be inferred that a carbo-hydrate enters into its composition. Chitin.

The analyses of chitin instituted by Schmidt and Lehmann differ very slightly from one another. From his analysis, Schmidt calculates for it the formula $C_{17}H_{14}NO_{11}$.

Chitin forms the true skeleton of all insects and crustacea, constituting not merely their external skeleton, but (in the case of insects) materially entering into the composition of the tracheæ and intestinal canal.

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(113.*) TABULAR VIEW OF THE PROXIMATE DERIVATIVES OF THE PROTEIN-BODIES.

| *Ossein* (*Fremy*). | | *Glutin yielded by it* (*Fremy*). | |
|---|---|---|---|
| Carbon . . . | 49·21 | Carbon . . . | 50·40 |
| Hydrogen . . | 6·50 | Hydrogen .. . | 6·50 |
| Nitrogen . . | 17·86 | Nitrogen . . | 17·50 |
| Oxygen . . . | 25·14 | Oxygen . . . | 26·00 |

| *Chondrin* (*Mulder*). | | *Chitin* (*Lehmann*). | |
|---|---|---|---|
| Carbon . . . | 49·97 | Carbon . . . | 46·73 |
| Hydrogen . . | 6·63 | Hydrogen . . | 6·59 |
| Nitrogen . . | 14·14 | Nitrogen . . | 6·49 |
| Oxygen . . . | 28·59 | Oxygen . . . | 40·18 |
| Sulphur . . . | 0·38 | | |

# CHAPTER IX.

## THE INORGANIC CONSTITUENTS OF THE ANIMAL BODY.

Inorganic constituents.

(114.) Our knowledge of the mineral substances occurring in organised bodies (whether plants or animals) is much less perfect than might be supposed would be the case, considering the general accuracy of inorganic analyses at the present day. The principal reason of this defective knowledge is, that we usually only attempt to determine these substances from the ash left on incineration,—a process which expels volatile acids and salts of ammonia, decomposes organic salts, and causes an almost complete re-arrangement of the various constituents, so that from the composition of the ash we are unable to draw any trustworthy conclusion regarding the exact nature of the pre-existing substances:* and, we may add as a secondary reason, that most of the analytical methods that have been applied to the investigation of the ashes of organic bodies, have not been of a nature to lead to very accurate results.

We may divide the mineral substances occurring in the animal body into three classes:—

* I may point out one or two of the chief causes of difference between the preformed mineral substances and those occurring in the ash. On incinerating a protein-body, or one of its proximate derivatives containing sulphur or phosphorus, this sulphur or phosphorus will pass into the ash in the form of sulphuric or phosphoric acid (in combination with a base), if there be free access of air during combustion. Again, at a very great heat, common phosphate of soda abstracts a portion of the base, not only from alkaline carbonates, but even from alkaline sulphates and chlorides, so that an ash may have lost all its alkaline carbonate and a portion of its hydrochloric and sulphuric acids.

Their division into three classes.

1. Those which are chiefly of service from their physical characters. In this class we especially include those which by their deposition give strength and power of resistance to the solid tissues.

2. Those which are chiefly of service from their chemical characters, taking an active part in the metamorphosis of tissue, and in the most important vital functions.

3. Those which are only incidentally retained in the organism, or which, originating in the metamorphosis of tissue, are to be regarded as mere products of excretion.

### SUBSTANCES USEFUL FROM THEIR PHYSICAL CHARACTERS.

Substances useful from their physical properties.

(115.) In this class we may place —

Water (which might equally be placed in the second class),
Phosphate of lime,
Carbonate of lime,
Phosphate of magnesia,
Fluoride of calcium, and
Silicic acid.

Water.

(116.) *Water* is a substance of whose uses in the animal organism it is superfluous to speak. The physical properties of many tissues depend upon the water which is mechanically combined with them. All chemical processes going on in the animal body require the co-operation of water; and the influence of this substance on nutrition and secretion is very marked, as will be shown in a future part of this volume.

Phosphate of lime.

(117.) *Phosphate of lime* affords the most striking illustration of this class of bodies, since it is to it that the osseous skeleton mainly owes its firmness and hardness. Thus, when too little phosphate of lime is taken into the system with the food (as in Chossat's well-known experiments), or when certain physiological processes make a special demand for this salt (as during pregnancy when the fœtal bones require it for

their ossification, and during the period of dentition), the bones lose more or less of their firmness, and fractures do not readily heal. In all diseases of bone there seems to be a greater relative diminution of this salt than of any other essential substance; but when the permanent cartilages undergo the change commonly described as ossification, they are found to contain an abnormal quantity of phosphate of lime.

Of all parts of the body the teeth are the richest in this substance, which is most abundant in the enamel.

There is some doubt as to the exact composition of the phosphate of lime occurring in these hard parts of the body. Berzelius was of opinion that it was represented by the formula $8CaO.3PO_5$; while Heintz, whose investigations were carried on under the superintendence of Rose, was led to regard $3CaO . PO_5$ as the correct formula.

Although there are no parts of the body in which phosphate of lime occurs near so abundantly as in the bones and teeth, yet there is no texture in which it is not present, or at all events which does not yield it on incineration. Liebig considers that the insolubility of various tissues, as, for instance, muscular fibre and connective tissue, in water, and their solubility in dilute hydrochloric acid (as in the digestive process) is, in a great measure, dependent on the phosphate of lime which they contain. Thoroughly dried muscular fibre contains about 1% of this salt.

Phosphate of lime occurs in solution in all the animal fluids, where it is generally (except in the urine) combined with the dissolved protein-bodies contained in them. There can be no doubt that it is chemically combined with them, and that it takes a part in the changes which they undergo, both in their progressive metamorphosis into tissue and in their regressive metamorphosis into products of excretion. The protein-bodies are thus the conveyers of the phosphate of lime to the cells and tissues. Among the various facts which may be brought forward in support of the view that phosphate

of lime is indispensable to cell-formation, we may mention that in the mantle of the molluscs (where new cells for the formation of shell abound) more of this salt is accumulated than is found in any other part of the animal.

A large quantity of phosphate of lime occurs in animal concretions, where it exists in an amorphous state. Schlossberger once found it in a crystalline form in a urethral calculus.

The quantity of phosphate of lime in the urine is dependent on the quantity of this substance occurring in the food, and on the demands of the organism for this salt. From the great demand on the part of the fœtus for this substance, we commonly find that, during the latter months of pregnancy, the urine hardly contains more than traces of it, even when the diet has been sufficiently abundant. In the urine of herbivorous animals it is very much less abundant than in that of the carnivora, because in the former the supply of calcareous salts, yielded by the food, scarcely exceeds the demands of the system.

Although by far the greatest quantity of the phosphate of lime found in the body has, doubtless, been introduced into the system from without, yet it is unquestionable that a portion of it is formed within the organism from other lime-salts (especially carbonate of lime) and from the phosphates which must be formed in the regressive metamorphosis of the phosphorus-containing tissues. This process of formation of phosphate of lime from its proximate constituents may be almost directly observed in the development of the chick within the egg, for it has been shown by Prout's observations that so much carbonate of lime is transferred, during incubation, from the shell to the yelk, as to explain the augmentation of the phosphate of lime (in so far as the lime is concerned) during the growth of the chick within the egg. The origin of the additional phosphoric acid is explained in this manner: part of the phosphorus of the yelk exists in the form of glycero-phosphoric acid, which, during incubation, becomes

gradually decomposed; so that the liberated phosphoric acid unites with the lime-salt, which we have already described as being transmitted from the shell to the yelk.

(118.) *Carbonate of lime* is the main ingredient of the shell of invertebrate animals; it likewise occurs in comparatively small quantity in the bones of the vertebrata; and in these cases it seems to serve the same purpose as phosphate of lime. Carbonate of lime.

It occurs in a state of solution, being dissolved by the free carbonic acid, in various animal fluids, as, for instance, in the parotid saliva (especially of the horse and dog), in the urine of herbivorous animals, and, probably, also in their blood. It is sometimes found in human urine with an alkaline reaction.

It is a very common constituent, in greater or lesser quantity, of many concretions.

The only part of the human organism in which it is said to occur normally, in a crystalline state, is in the saccule of the vestibule of the internal ear.

In many cases there can be no doubt that the carbonate of lime is a mere product of incineration; but, independently of this possible source of error, we have sufficient evidence that this salt actually exists in the tissues and fluids which we have named. Its origin must be chiefly referred to our vegetable food, and to the water used for drinking; it is possible, however, that it may also be formed, to a certain extent, in the blood by the decomposition of organic lime-salts.

Its solubility in the animal fluids has been variously explained. Free carbonic acid is, probably, its ordinary solvent; but it is also more or less soluble in solutions of the alkaline chlorides and of various organic matters, as, for instance, sugar.

(119.) *Phosphate of magnesia*, in small quantity, is always associated with phosphate of lime, and, like the latter salt, occurs chiefly in the bones. Phosphate of magnesia.

It is proved by ash-analyses that a little phosphate of magnesia is present in all animal fluids and tissues; and a still more simple evidence of its existence is afforded by allowing them to undergo decomposition, when, on the development of ammonia, the well-marked crystals of phosphate of ammonia and magnesia may be recognised by the microscope (*Pl. IV. fig. 5.*).

It is found in the fæces in relatively larger quantity than phosphate of lime, which led Berzelius to the idea that the lacteals were less disposed to absorb the magnesian than the lime-salt. There is, however, no necessity for such a hypothetical explanation, for, independently of the fact that a considerable quantity of phosphate of magnesia is absorbed by the intestine, as is evidenced by its presence in the urine, its tendency to form an insoluble crystalline salt with ammonia (which is always found in the fæces, and often forms large intestinal concretions in herbivorous animals) would suffice to explain its comparative abundance in the excrements.

The abundance of this salt in the seeds of the cereals and in the other ordinary articles of vegetable diet sufficiently explains its presence in the system. A far less amount of this salt than of the corresponding lime-salt seems to be required by the organism, as is shown by the relative quantities in which they occur in bone; and, as is further indicated by the fact, that far more of this than of the lime-salt escapes intestinal absorption.

Fluoride of calcium.

(120.) *Fluoride of calcium* occurs in minute quantity in the bones and teeth. It is usually much more abundant in these parts in fossil than in recent animals: it is very probable, however, that this excess is dependent on a process of infiltration rather than on an original peculiarity in the composition of the textures.

It has been shown by Professor George Wilson* that dis-

* Although these researches were published more than ten years ago, and the results noticed in many of the scientific journals of the time, M. Nickles, a

tinct traces of this substance may be exhibited in the blood, milk, &c.

The origin of this substance must be referred to the food. Many mineral waters contain traces of fluorides, and it is possible that vegetables may also take up a little of it from the soil.

(121.) *Silicic acid* forms the groundwork of the shields of many of the infusoria in the same manner that phosphate and carbonate of lime are the means of affording strength and resisting power to the bones of the vertebrata and shells of molluscs and crustaceans. Silicic acid.

In the higher animals it appears to be an integral constituent of feathers, wool, and hair. Small quantities of it have been found in the blood and in the eggs of birds; and traces of it have occasionally been detected in the blood, bile, and urine of man and various animals.

In the solid excrements we always find silicic acid, partly in the form of actual sand, and partly derived from the vegetable tissues of the food.

### SUBSTANCES CHEMICALLY SERVICEABLE.

(122.) In this group we place: —

Hydrochloric acid,
Chloride of sodium,
Carbonate of soda,
The alkali-phosphates,
Ammonia and its salts, and
Iron.

(123.) *Hydrochloric acid* never occurs free except in the gastric juice, and even there it possibly exists as a conjugated Hydrochloric acid.

French chemist, has recently announced the presence of fluorine in the blood as a new fact of his own discovery. See the Philosophical Magazine, March, 1857.

acid (see the Chapter on "The Gastric Juice"). Unless the gastric juice be distinctly acid it does not possess its characteristic digestive action; and the only acid which can physiologically replace hydrochloric acid in this fluid is lactic acid.

By what chemical process the hydrochloric acid is liberated in the gastric glands is at present unknown.

Chloride of sodium.

(124.) *Chloride of sodium* is a substance whose importance, in relation to the metamorphosis of the tissues, is clearly shown by the fact of its occurrence in all the animal solids and fluids, in the latter of which (if we except the expressed juices of the muscular tissue and of the thymus gland, and the yelk of egg) it forms the greater part of the soluble ash-constituents; and, by the circumstance that its amount in the blood is nearly constant, whatever may be the quantity of salt taken with the food. The influence of this salt in modifying the characters of the protein-bodies is very remarkable; it augments the solubility of albumen, and the coagulation of this substance varies with the amount of salt that is present; it acts as a solvent to pure casein, and hinders, in an extraordinary degree, the coagulation of the fibrin of the blood. There is no certain evidence that it enters into chemical combination with these bodies, but it is more than probable that it does so, from the influence which it exerts on them, from the analogous compound which it forms with glycose, and from the impossibility of separating it from them by mere washing. It would also seem as if active cell-formation specially required the presence of salt; at all events cartilage, which in its perfectly developed stage is singularly rich in cells, contains more of this substance than any other tissue; and the cartilaginous bones of the fœtus, in which there is comparatively little deposition of phosphate of lime, contain far more salt than the bones of the adult.*

* Lehmann found that the laryngeal cartilages of an adult woman yielded an ash containing 11 236 of chloride of sodium; and while various adult

The following table gives, at a glance, the relative quantities of chloride of sodium contained in the chief animal fluids; *a* represents the per-centage in the fluid itself, *b* in its solid residue, and *c* in the ash: —

| | *a.* | *b.* | *c.* |
|---|---|---|---|
| Human blood (L.) * . . | 0·421 | 1·931 | 57·641 |
| Blood of horse (L.) . . | 0·510 | 2·750 | 67·105 |
| Blood of cat (N.) . . | 0·537 | 2·286 | 67·128 |
| Chyle of horse (L.) . . | 0·531 | 8·313 | 67·884 |
| Chyle of cat (N.) . . | 0·710 | 7·529 | 62·286 |
| Human saliva (L.) . . | 0·153 | 12·988 | 62·195 |
| Human mucus (N.) . . | 0·583 | 13·100 | 70·000 |
| Serum of pus (N.) . . | 1·260 | 11·454 | 72·330 |
| Pleuritic exudation (S.) . | 0·750 | 10·416 | 73·529 |

The sources from whence we derive the salt found in the body are too obvious to require notice.

The uses of this substance will be fully considered in the Chapter on "The Metamorphosis of the Tissues."

Carbonate of soda.

(125.) *Carbonate of soda* is an ordinary ingredient of the ash yielded by the combustion of organic matters; in this case it is, however, usually only a product of decomposition, induced by a high temperature on the compounds of soda with organic acids or with the protein-bodies. It has been proved to exist preformed, in combination with other soda-compounds, in the blood and in the lymph. (As a mean of ten experiments, Lehmann found 0·1628% of carbonate of soda in ox-blood, and Nasse found 0·056% in the lymph of a horse). It occurs in the urine of herbivorous animals in association with the carbonates of potash and lime.

The uses of this salt in the blood and other fluids will be

bones yielded only from 0 7 to 1·5%, the femur of a six-months' fœtus yielded 10·138%.

* In the above table (L.) indicates that the analysis was made by Lehmann, (N.) by Nasse, and (S.) by Scherer.

noticed in the Chapter on "The Metamorphosis of the Tissues;" the principal object which it effects in the blood, probably, is to neutralise the acids conveyed into or developed within the organism.

Phosphates of the alkalies.

(126.) The *alkali-phosphates* are found in most of the animal fluids, where, however, they occur in very different quantities, as may be seen by a reference to the subjoined table. It is worthy of notice that they seem to stand in an inverse ratio to the chloride of sodium, in the same manner as the potash-salts preponderate where the soda-salts are scanty. Thus they are in excess in the blood-corpuscles, in the yelk of egg, and in the expressed juices of the muscular tissue and of the thymus gland, and are found in only small quantities in the alkaline fluids, as the serum of the blood, the white of egg, &c. As they occur chiefly in acid fluids, we must conclude that the acid phosphate of potash is the principal alkali-phosphate in these cases.

The quantity in which they exist in the urine varies partly with the amount in which they occur in the food, and partly with the rapidity of the regressive metamorphosis of the tissues, in which the phosphorus of the organic matters becomes oxidised into phosphoric acid, which at once unites with alkaline bases. The following results were obtained from analyses made in Rose's laboratory at Berlin; *a* represents the soluble salts in 100 parts of ash, and *b* the percentage of alkali-phosphates in *a*:—

| | *a.* | *b.* |
|---|---|---|
| Ox-blood . . | 60·90 | $3KO.PO_5$ = 1·58 |
| Horse-flesh . . | 42·81 | $2NaO.PO_5$ = 11·10<br>$2KO.PO_5$ = 83·27 |
| Cows'-milk . . | 34·17 | $3KO.PO_5$ = 21·60 |
| Yelk of egg . . | 40·95 | $KO.PO_5$ = 24·57<br>$NaO.PO_5$ = 25·16 |

| | *a.* | *b.* |
|---|---|---|
| White of egg . . | 81·85 | 0·00 |
| Ox-bile . . . | 90·85 | $3KO.PO_5 = 6·78$<br>$3NaO.PO_5 = 14·51$ |
| Urine . . . | 90·87 | $2KO.PO_5 = 16·12$<br>$3KO.PO_5 = 4·55$ |
| Solid excrements | 18·55 | $3KO.PO_5 = 20·13$ |

The uses of the alkali-phosphates will be seen in our remarks on Exudations, and on the Metamorphosis of the Tissues.

(127.) *Ammonia* and its *salts* have been regarded by all recent chemists as of much more rare occurrence in the organism than was formerly supposed. Ammonia and its salts.

According to Lehmann, the blood, chyle, lymph, milk, and fluids of the egg contain, in their normal state, either no ammonia or only most minute traces of it; but in certain diseased conditions, especially in typhus, variola, and scarlatina, it has been shown by Winter and others to occur, as a carbonate, in the blood in considerable quantity.

Dr. Richardson, in his Astley Cooper Prize Essay, has, however, announced the startling discovery that ammonia is the agent which retains the fibrin of the circulating blood in a state of solution, and that on its exhalation as the blood is exposed to the air, in the process of being abstracted, the precipitation of the fibrin depends.

I am indebted to the kindness of Dr. Richardson for an account of the following beautiful experiment, showing the presence of ammonia in the blood. On moistening the interior of the surface of a cupping-glass with a little hydrochloric acid before applying it to the incised part, we find that, as the escaping blood exhales its gases, patches of crystals of hydrochlorate of ammonia, visible to the naked eye, and of whose microscopical characters and chemical constitution there can be no doubt, are formed in the upper part of the glass.

It has been established by Marchand, Reuling, and others, that ammonia is present in the pulmonary exalation, and it was also known as a constituent of the urine; Dr. Richardson proves that it is likewise given freely off by the skin, and that it may be detected in the saliva and the serous fluids.

In cases of advanced albuminuria, carbonate of ammonia, arising from the decomposition of non-eliminated urea, is found in the gastric juice. Many pathologists now hold that the comatose symptoms which occur in the last state of uræmia are due not to urea, but to carbonate of ammonia, accumulating in the blood.

It is almost unnecessary to observe that ammoniacal salts are developed during the decomposition of almost all the tissues.

Iron.

(128.) *Iron* is found in different states of combination in different parts of the animal body. In the hæmatin of the blood it seems to exist in an unoxidised state in combination with the other organic elements of that pigment, while in the gastric juice it is found as a protochloride, and in other fluids, as, for instance, the splenic juice, as a phosphate of the peroxide. We are altogether ignorant of the part which it plays in the animal economy, but its occurrence in the ashes both of milk and of the egg indicates the importance of its function.

Any excess of iron in the system is, probably, eliminated by the liver and the hair-follicles; considerable quantities of it being found in the ashes both of bile and hair.

Its origin must be referred to the iron contained in our food, and frequently in the water that we drink.

SUBSTANCES INCIDENTALLY PRESENT.

(129.) In this group we place: —

The alkali-sulphates,
Carbonate of magnesia,
Manganese,
Arsenic,
Copper and lead, and
Sulphocyanides of potassium and sodium.

Sulphates of the alkalies.

(130.) The *alkali-sulphates* occur in considerable, but in very fluctuating quantity in the urine, in only a small quantity in the blood, and are not to be detected in the milk, in the fluids of the egg, in the gastric juice, or in the bile. It is true that the ashes of blood and of other fluids rich in protein-bodies usually yield considerable quantities of the alkali-sulphates, but these are, for the most part, formed during the process of incineration by the oxidation of the sulphur. Any excess of these salts in the blood seems to be at once carried off by the kidneys.

The circumstances modifying the quantity of alkali-sulphates in the urine will be noticed in the chapter on the fluid.

It has been ascertained by von Bibra that the bones of reptiles and fishes present the peculiarity of containing considerable quantities of sulphate of soda.

It has been shown by experiment that small quantities of alkali-sulphates are converted in the intestinal canal into the corresponding sulphides (sulphurets), and hence it might be inferred that these salts contributed to the formation of such animal substances as contain sulphur, as, for instance, horny tissue, although their formation may be otherwise (and perhaps more correctly) explained when we recollect that many articles of food contain unoxidised sulphur which might be

thus employed. The absence of alkali-sulphates, both in milk and in the fluids of the egg, seems to indicate that they do not take any very active part in the development of the textures.

Carbonate of magnesia.

(131.) *Carbonate of magnesia* occurs very sparingly in the bones, teeth, and egg-shells; but is often found in considerable quantity in the urine of herbivorous animals. It has been not unfrequently observed in animal concretions of various kinds. As the only magnesian salt found in the cereals and grasses is the phosphate, it is more than probable that the carbonate found in the urine of the herbivorous animals is formed within the organism (either in the blood or in the tissues during their regressive metamorphosis) by the action of organic lime-salts on phosphate of magnesia, the resulting magnesian salt (malate, tartrate, &c.) being reduced in the blood to a carbonate.

Manganese.

(132.) *Manganese*, the almost universal associate of iron, is found in small quantities in those parts of the organism in which iron normally occurs, especially the blood and hair. Like most of the metals, its excess is eliminated by the liver, and hence we find it in a larger proportion in the bile than elsewhere. Burin du Bouisson found that on an average human blood contains 0·0078% of red oxide of manganese, $Mn_3O_4$, while the average percentage of iron is 0·05; in the bile, on the other hand, Weidenbusch found that red oxide of manganese stood to the peroxide of iron in the ratio of 1 : 2.

It is occasionally a constituent of gall-stones, and has been found in urinary calculi.

Arsenic.

*Arsenic* was at one time regarded (especially by Devergie and Orfila) as a normal constituent of the bones; but this view has been since proved to be erroneous. From experiments on animals (chiefly horses and rabbits) it appears that arsenic, when given in considerable doses, is rapidly eliminated by the great excreting organs, the liver and kidneys, and that, consequently, it is found most abundantly in their tissues and

in the fluids which they secrete; it may likewise be found in lesser quantities in the heart, lungs, brain, and muscles; but it does not enter the osseous tissue.

Copper and lead.

*Copper* and *lead* have no more claim than arsenic to be regarded as normal constituents of the human body. After their administration (either medicinally or accidentally) they are retained for some time in the system, and are finally eliminated by the liver; hence they are more frequently found in the bile and in gall-stones than elsewhere. Copper is, however, an ordinary constituent of the blood and of the liver of numerous of the invertebrate animals (crustaceans, cephalopods, ordinary molluscs, and ascidians).

Sulphocyanogen.

(133.) *Sulphocyanogen*, in combination with potassium or sodium, has, as yet, only been found in the saliva. It has been detected in this secretion in man (in whose saliva it usually, but not invariably occurs), in the dog, and in the sheep; the evidence regarding its presence in the saliva of the horse is contradictory, Lehmann having failed to detect it. Its origin is, unquestionably, dependent on some special decomposition of the tissues with which we are at present unacquainted; and the only suggestion regarding its use is the very improbable one that it may check the formation of minute fungi on the buccal mucous membrane (Kletzinsky).

END OF BOOK I.

# BOOK II.

THE

# CHEMISTRY OF THE ANIMAL JUICES AND TISSUES.

# BOOK II.

(134.) THE leading fluids or juices of the animal body admit of a natural division or classification into the five following groups: — Classification of the subject.

I. The *digestive fluids*, including the saliva, gastric juice, bile, pancreatic fluid, and intestinal juice; and to these we have added the consideration of the intestinal contents.

II. The *blood and its allies*, including the chyle, the lymph, the blood itself, and the various transudations.

III. The *fluids connected with generation and development*, including the seminal fluid, the milk, and the fluids of the egg.

IV. The *excretions of the mucous membrane and the skin*, including mucus, the various sebaceous matters, and the sweat.

V. The *urine*.

After the consideration of these normally existing fluids we shall notice those *Exudations* which are occasionally found, as products of disease, in the animal organism, and shall conclude this Book with a few remarks on the Chemistry of the *Solid Tissues* of the Body.

# CHAPTER X.

## THE DIGESTIVE FLUIDS.

### SECTION I.—THE SALIVA.

Saliva.

(135.) The saliva, in the ordinary acceptation of the term, is a mixture of the secretions of the three pairs of salivary glands and of the buccal mucus. It is a colourless, or very faintly blue, turbid, viscid, inodorous, and tasteless fluid, which, after standing for some time, separates into an upper transparent layer, and a lower, opaque, yellowish-white portion, consisting of pavement epithelium and mucus-corpuscles. In the normal state its reaction is always alkaline, but the degree of alkalinity varies, and is found to increase during and after meals; while after prolonged fasting the secretion is almost neutral. The specific gravity of human saliva was determined by Jacubowitsch at 1·0026, and, after the deposition of the sediment, at 1·0023. Lehmann states that its usual variations in man are between 1·004 and 1·006, its extreme normal limits being 1·002 and 1·009; while Wright, our principal English experimenter on the saliva, asserts that in numerous experiments made on two hundred healthy persons, the specific gravity varied from 1·0069 to 1·0089. Lehmann may be regarded as giving the safest estimate.

We shall now consider, individually, the various secretions which collectively form the mixed saliva.

Parotid saliva.

(136.) The *parotid saliva*, which can only be obtained from artificial or spontaneous fistulous openings in Steno's duct, is limpid and colourless, devoid of smell and taste, not viscid, has a specific gravity varying from 1·0061 to 1·0088 in man

(Mitscherlich), from 1·004 to 1·007 in the dog (Schmidt), and from 1·0051 to 1·0074 in the horse (Lehmann); and is distinctly alkaline in its reaction.

The following may be regarded as the normal constituents of this secretion: —

(*a.*) An organic matter, named *ptyalin*, very similar to, but not identical with albuminate of soda, and occurring in combination with potash, soda, and lime. It is a gelatinous matter, which is soluble in water, especially when in combination with an alkali, and does not coagulate on heating. That portion of it which is combined with lime is soon displaced by carbonic acid, and the originally limpid secretion becomes turbid on exposure to the air in the same manner as lime-water. With this there is associated another organic matter, which merely differs from it in not being precipitable by alum, and which has received no special name. Ptyalin.

(*b.*) A potash-salt of the volatile acids belonging to the butyric-acid group, probably caproic acid. It crystallises in beautiful tufts like margaric acid.

(*c.*) Sulphocyanide of potassium has been found in the parotid saliva of man and various of the domestic mammals.

(*d.*) In the ash there are found considerable quantities of the chlorides of sodium and potassium, some carbonate of lime, and small quantities of phosphates.

In 1000 parts of the parotid saliva of a dog, Schmidt found: —

| | |
|---|---|
| Water . . . . . | 995·3 |
| Solid residue . . . . . | 4·7 |
| Organic matter . . . . . | 1·4 |
| Alkaline chlorides and sulphocyanides | 2·1 |
| Carbonate of lime . . . . . | 1·2 |

In man the percentage of the solid constituents seems higher than in the dog, Mitscherlich fixing it at from

1·468 to 1·632%, and van Setten at 1·62% (which is three times as high as in the dog).

Submaxillary saliva.

The *submaxillary saliva* is a clear, colourless, very viscid fluid, without smell or taste; in the dog (and this is the only animal in which this secretion has been carefully examined) the specific gravity was found to vary from 1·0026 to 1·0041 (Schmidt). Its reaction is less strongly alkaline than that of the parotid; and it contains the same constituents as the latter (including sulphocyanide of potassium), but less lime in combination with organic matter.

Schmidt has given the two following analyses of this secretion in the dog:—

| | (1.) | (2.) |
|---|---|---|
| Water . . . . . | 996·04 | 991·45 |
| Solid residue . . . . . | 3·96 | 8·55 |
| Organic matter . . . . | 1·51 | 2·89 |
| Inorganic matters . . . | 2·45 | |
| Chlorides of sodium and potassium . . | | 4·50 |
| Carbonate and phosphate of lime and phosphate of magnesia . . . | | 1·16 |

The great difference of the solid residue in these cases is dependent on the fact that in the former 25·23 grammes of saliva were secreted in one hour, while in the latter only 13·6 grammes were yielded in the same time; so that the absolute quantity of solid residue is nearly the same in both cases. Hence we may infer, that when there is a great augmentation of the secretion, it is due almost solely to an excess of water.

Sublingual saliva.

The *sublingual saliva* has never been separately analysed; most of these observations having been made on dogs, which do not possess sublingual glands.* Longet has recently shown

* This is the view generally held by comparative anatomists. Bernard, however, maintains that in dogs and other carnivora there is a sublingual gland in close contact with, but distinct from the submaxillary gland.

that, like parotid and submaxillary saliva, it contains sulphocyanogen.

(137.) The *secretion of the buccal mucous membrane*, mixed, however, with the secretion of the orbital glands, has been examined in dogs (by Jacubowitsch). It is a very tough and viscid fluid, colourless, but turbid from the presence of epithelial cells, and alkaline in its reaction. Its solid residue amounts to about 1%, in which about ·61 is inorganic matter. Buccal mucus.

(138.) After this sketch of the physical and chemical characters of the individual fluids which collectively form the ordinary or mixed saliva, we have little to add to the observations in § 135. regarding its physical and chemical characters.

In the following table we give the chemical composition of healthy human saliva, as determined by Frerichs and Jacubowitsch (under Schmidt's superintendence): — Composition of mixed saliva.

| *Frerichs.* | | *Jacubowitsch.* | |
|---|---|---|---|
| Water . . . . | 994·10 | Water . . . . | 995·16 |
| Solid constituents . | 5·90 | Solid constituents . | 4·84 |
| Epithelium and mucus | 2·13 | Epithelium . . | 1·62 |
| Fat . . . . | 0·07 | | |
| Ptyalin with a little alcohol extract . | 1·41 | Soluble organic matter . . . | 1·34 |
| Sulphocyanide of potassium . . | 0·10 | Sulphocyanide of potassium . . | 0·06 |
| Fixed salts . . | 2·19 | Fixed salts . . | 1·82 |

The "soluble organic matter," in the second analysis, is probably a mixture of ptyalin and of mucin, an ill-defined soluble organic matter occurring in mucus; and the 1·82 parts of fixed salts consisted of phosphate of soda 0·94, lime 0·03, magnesia 0·01, and the chlorides of sodium and potassium 0·84.

The presence of sulphocyanide of potassium is interesting, insomuch as the saliva is the only fluid in which sulpho

cyanogen seems normally to occur; and it is evident, from the above analyses, that even here it exists in only very small quantity. Lehmann found it to vary in his own saliva from 0·0046 to 0·0089 per cent. Kletzinsky * has examined the conditions under which this constituent occurs in augmented or diminished quantity in the saliva, and he believes that its use is to prevent fermentation and the development of fungoid spores; and Herapath † has shown that the amount of sulphocyanogen in the saliva, even of the same individual, is liable to great fluctuations.

It is worthy of notice that the two latest observers who have taken up this subject, and whose researches were published in 1855, arrived at entirely contradictory results. Longet maintains that sulphocyanides are invariable constituents of the secretions of all the salivary glands, while Kölliker and H. Müller failed in detecting any trace of them in the parotid and submaxillary fluids of the dog.

Abnormal saliva.

(139.) Various *incidental* ‡ and *abnormal* constituents are frequently to be detected in the saliva. Amongst the former we may place iodine, bromine, and mercury, when these substances are used medicinally §; while, amongst the latter, we may mention some of the constituents of the bile (including cholesterin), sugar, and possibly albumen.

* Heller's Archiv f. Phys. u. Path. Chemie, 1853, p. 39. I have given his principal conclusions in "The Chemistry of Digestion," in the British and Foreign Medico-Chir. Rev., 1853, vol. xii. p. 168.

† His results are given in my "Report on the Progress of Animal Chemistry during the Years 1852-3-4," in the British and Foreign Medico-Chir. Rev., 1855, vol. xv. p. 549.

‡ By *incidental* constituents we mean those which owe their origin to an introduction from without, while we confine the term *abnormal* to those matters which are generated within the organism. Strictly speaking, the former are included in the latter.

§ Bernard has shown that the salivary glands and other secreting surfaces exercise an elective elimination on foreign materials introduced either directly or by absorption into the blood. Thus, he detected iodide of potassium in the saliva, pancreatic juice, and tears, in less than one minute; but in the urine and bile, not till an hour after their injection. Lactate of iron furnishes no iron to the saliva, but when iodide of iron is administered both constituents can be recognised in that secretion.

Acid saliva is occasionally observed; it seems chiefly to occur in cases of irritation of the primæ viæ and of diabetes mellitus; but we do not know on what the acid reaction depends, and, indeed, our knowledge of the pathological conditions of the saliva is extremely imperfect.

Salivary concretions.

(140.) Salivary concretions must be included amongst the morbid products of this secretion. They have been frequently analysed, and are found to contain more carbonate of lime than any other kind of concretion. In the following table, which will give a fair idea of their quantitative composition, the first three analyses were made by Wright, the fourth by von Bibra, and the fifth by Lecanu: —

| | (1.) | (2.) | (3.) | (4.) | (5.) |
|---|---|---|---|---|---|
| Carbonate of lime . | 81·3 | 79·4 | 80·7 | 13·9 | 20 |
| Phosphate of lime . | 4·1 | 5·0 | 4·2 | 38·2 | 75 |
| Phosphate of magnesia | — | — | — | 5·1 | — |
| Soluble salts . . . | 6·2 | 4·8 | 5·1 | 38·1 | |
| Animal matter . . | 7·1 | 8·5 | 8·3 | | |
| Water and loss . . | 1·3 | 2·3 | 1·7 | 6·3 | 5 |
| | 100·0 | 100·0 | 100·0 | 100·0 | 100·0 |

Quantity of saliva.

(141.) The daily quantity of saliva secreted by an adult man has been variously estimated (by Burdach, Valentin, Donné and Thomson) at from 210 to 390 grammes (or from about 6·5 to 12 ounces). From the recent investigations of Bidder and Schmidt it appears, however, that these estimates are far too low, and that an adult man secretes, on an average, 1500 grammes or about 48 ounces daily.

All such determinations as these must, however, be regarded only as approximations to the truth, since the activity of the salivary glands is dependent upon various influences and conditions. Movement of the lower jaw increases the flow of saliva; hence mastication, speaking, and singing, augment the secretion. Acid, aromatic, and irritant sub-

stances produce a similar effect. Dry and hard food causes an abundant flow, while the use of moist and soft food is accompanied by a scanty secretion. Thus it appears, from the observations of Bernard and others on horses, that straw and hay, as they pass down the œsophagus, are mixed with four or five times their weight of saliva, while seeds abounding in starch, as, for instance, oats, are mixed with not more than one and a half times their weight of saliva; and fresh green fodder with only half its weight; while food, mixed with water, seems to take up scarcely any saliva. Corresponding observations have since been made on the ox by Colin.

Some very interesting experiments on the influence of the period of secretion on the constitution of the saliva have been made by Becher and Ludwig. They found that the solid residue of the saliva diminishes in proportion to the amount which the gland has already yielded; the organic constituents sinking far more rapidly than the inorganic.

Its functions.

(142.) The functions of the saliva are partly of a mechanical and partly of a chemical nature.

Mechanical uses.

The mechanical uses of the saliva are almost too apparent to require notice. It is obvious that the moistening of dry food, by the process of insalivation, serves the double purpose of adapting it for deglutition and of separating the particles and thus allowing them to be more freely acted on by the other digestive fluids. Bernard believes that the parotid and submaxillary fluids discharge independent functions — that the parotid, by its thin fluid property, serves to moisten the food, while the tough and viscid secretion of the submaxillary glands is specially subservient to the sense of taste, and, at the same time, lubricates the bolus, and thus facilitates deglutition. Liebig has suggested that the saliva, from its tendency to frothing, may be designed to convey air into the stomach and intestines; it would appear, however, from the investigations of Wright, Valentin, and others, that the presence of oxygen is not necessary for gastric digestion.

(143.) It is now almost universally admitted that the principal use of the salivary secretion is to promote the conversion of the amylaceous portion of the food into dextrine, sugar, and lactic acid, and thus to promote its absorption. Chemical uses.

The first point to be noticed is the time required for the metamorphosis of starch by ordinary (or mixed) human saliva. If we take a decoction of starch, prepared with distilled water and proved by Trommer's test to be free from sugar, and if we mix it with an equal quantity of fresh saliva, and agitate the mixture, it will instantly lose its viscid character and become thin and watery; and, on testing a small quantity of it for starch, we find that iodine no longer induces the well-known reaction, while, on the other hand, the rapid reduction of oxide of copper (in Trommer's test) affords indisputable evidence of the presence of sugar. The almost instantaneous induction of this action is a point which must not be overlooked in considering the question, whether this is a special property of the saliva, or whether it is shared by other animal fluids. There can be no doubt, as will be presently shown, that in this respect the pancreatic and intestinal juices exactly coincide with the saliva; but when we find stress laid upon the circumstance that many other organic substances — as, for instance, nasal mucus, pieces of kidney, putrefying serum, &c., produce similar changes in eight or twelve hours at 100° or upwards, we must recollect that at such a temperature, and after so long an interval, changes may be spontaneously set up in a solution of starch. There are, however, a number of animal substances which occasion the appearance of sugar in a solution of starch in so short a period as altogether to exclude, in such cases, the suspicion of spontaneous metamorphosis; but the action induced by the saliva is incomparably more rapid even than that of any of these substances.*

* I have given a list of these substances (from Bidder and Schmidt), in "The Chemistry of Digestion," in the British and Foreign Medico-Chir. Review, 1853, vol. xii. pp. 172, 173.

The question regarding the part which the various secretions, entering into the composition of the saliva, take in this action is a comparatively recent one, and much light has been thrown upon this subject by the investigations of Bernard, Jacubowitsch, Bidder and Schmidt, and others. The first step in this direction seems to have been made by Magendie and Rayer, who ascertained that the parotid secretion of the horse exerted no metamorphic action on starch; and Bernard has subsequently demonstrated the same thing with the parotid, submaxillary, and sublingual secretions of the dog, showing that these fluids, either separately or mixed, exert no action on amylaceous matters. Hence Bernard concludes that the conversion of starch into sugar depends solely upon the secretion of the buccal mucous membrane — a view which is supported by the circumstance that the fluid obtained by macerating this membrane in water possesses, after filtration, the power of effecting this change. Since, however, it might be objected that some of the salivary secretion might adhere to the buccal mucous membrane, Bidder and Schmidt tied the salivary ducts of a dog, and a fortnight afterwards found that neither the buccal mucus nor the aqueous extract of the detached buccal mucous membrane exerted any marked change on a solution of starch — results by no means in accordance with Bernard's views. As the accuracy of this statement, as originally promulgated by their pupil, Jacubowitsch, was impugned by Frerichs, they instituted new experiments, and obtained not only the pure secretions of the parotid and submaxillary glands, but also the pure secretion of the buccal mucous membrane of dogs. The secretions thus obtained were individually mixed with a solution of starch and exposed to a temperature of 104°. In no case was sugar detected sooner than in eight hours, and then only in mere traces, and hence they consider it as unquestionably established that the ferment, on which the conversion of starch into sugar depends, is not contained in any single one of the

secretions by whose admixture the ordinary saliva is formed, and that it has its source solely in the admixture of some or all of these secretions.

The next question is — Are all the three secretions (those of the parotids, the submaxillaries, and the buccal mucous membranes, for that of the sublingual glands is neglected by most of these observers as unworthy of notice) of equal importance in producing the final result, or would the admixture of two of these be sufficient? Jacubowitsch performed some admirable experiments which, in themselves, seem to answer the question definitely, although, in one important point, they have not been confirmed by the subsequent observations of Bidder and Schmidt. He convinced himself, by preventing the parotid and submaxillary fluids from entering into the mouth of a dog, that the mere secretion of the mucous membrane of the mouth (contrary to Bernard's assertion) was unable to convert starch into sugar. But when he tied the ducts of only a single pair of glands (either of the two parotids or the two submaxillaries), and then, after the recovery of the dog, digested starch with the saliva that exuded from its mouth, some of the starch was converted into sugar in the course of five minutes. Starch was also quickly changed when brought in contact with an artificial mixture of either of the above-named glandular secretions and buccal mucus; while a mixture of the parotid and submaxillary fluids, without any secretion from the mucous membrane, was entirely deficient in this property. The only point in which Bidder and Schmidt, in their subsequent experiments, differ from Jacubowitsch, is that, according to them, parotid saliva mixed with pure buccal mucus exerts no marked action on the conversion of starch into sugar. They are unable to account for this difference in any satisfactory manner. They found that a mixture of the secretion of the submaxillary glands with pure buccal mucus exerted as rapid and perfect a metamorphosis of starch as the ordinary saliva.

The following are the two principal conclusions at which Bidder and Schmidt have arrived in connection with this point: —

1. They agree with Bernard in regarding the parotids as *glandes aquipares;* in short, as yielding a secretion which is unquestionably intended to moisten and saturate the dry food, but they believe that its principal object is connected with the general metamorphosis of the fluids within the body.

2. They consider that the peculiar ferment which almost instantly converts starch into sugar is formed by the union of the submaxillary secretion and that of the buccal mucous membrane, the parotid secretion taking no part whatever in this process. This active principle is not contained in the cells or other solid particles suspended in the saliva; for the filtered fluid exhibits an undiminished force, and, indeed, this property is not destroyed when, by the addition of a little alcohol, we precipitate the mucus and (entangled with it) these solid particles.

Salivary secretion in infancy.

(144.) Another subject examined by Bidder and Schmidt is the condition of the salivary secretion during the period when the infant or the young animal continues sucking. Although, to all appearance, there is no special retardation of the development of the tissues of these glands, yet at this time they yield scarcely any secretion. This was demonstrated in the following ways:—(1.) On establishing fistulous openings in connection with Steno's duct in calves, no fluid escaped through the canula. (2.) Starch was converted into sugar in the presence of portions of the parotid or submaxillary glands of adult animals in a far shorter period than when the corresponding parts of sucking animals were used. And (3.) when the saliva of an adult man and the fluid from the mouth of an infant were mixed with equal parts of a thick solution of starch, the metamorphic action *commenced* in equally short spaces of time, that is to say, almost instantly in both cases; but, in the former case, the

action was completed almost as soon as it was begun, while, in the latter, the process occupied fully an hour.

Action of saliva in the stomach.

(145.) Formerly much importance was attached to the alkalinity of the saliva (which, by the way, seems rather to be due to the presence of an alkaline phosphate of soda than to that of a free alkali), and it was regarded as an established fact, that the special functions of this secretion must be altogether suspended when it entered the stomach and was mixed with the acid gastric juice. Although it seems universally admitted that the addition of acid gastric juice to the saliva in sufficient quantity to make the mixture acid has little or no effect on the metamorphic action on starch *out of the body*, there is still considerable doubt whether the action of the saliva on starch is continued *in the stomach*.

Jacubowitsch relates that he made the following mixtures and treated them with a fresh decoction of starch: —

(*a.*) Pure filtered gastric juice (obtained from a dog with a gastric fistula) was neutralised by human saliva; (*b.*) in another instance it was rendered alkaline by an excess of saliva; (*c.*) in a third case it was rendered alkaline by soda; (*d.*) saliva was rendered acid by gastric juice; (*e.*) pure gastric juice was finally mixed with starch.

These mixtures were kept at a temperature varying from 86° to 104°; and all of them, excepting *c.* and *e.*, exhibited distinct traces of sugar in the course of fifteen minutes.

These experiments show, as Jacubowitsch observes, that the gastric juice does not in itself impede the metamorphic action of saliva on starch; and further that the former secretion, even when neutralised with an alkali, possesses no such property. Bidder and Schmidt speak quite as decisively. "New experiments (they observe) have convinced us that the metamorphic action of the saliva in the presence of free acids exhibits itself with quite the ordinary rapidity. We have added to fresh human saliva enough acid gastric juice obtained from dogs, or enough hydrochloric acid, to render the

mixture neutral or acid, and have found that this mixture caused as immediate a conversion of starch into sugar as when pure alkaline saliva had alone been added."

Now since the gastric fluid may be regarded as a natural mixture of the swallowed alkaline saliva with the acid gastric juice, in which, however, the acid character normally prevails, it might be expected that it would exert the same metamorphic action on starch as the artificially acidulated saliva. This, however, is a warmly disputed point, Blondlot, Bouchardat and Sandras, and Bidder and Schmidt, maintaining, from their researches on the lower animals (dogs, sheep, and rabbits), that no conversion of starch into sugar takes place within the stomach; while Frerichs, in at least fifty experiments, constantly found sugar in the filtered contents of the stomachs of men, carnivorous and omnivorous mammals, and birds; and von Schröder, by his observations on a woman with a gastric fistula, seems to have established the point (in so far as man is concerned) beyond all cavil. In experiments *out of the body*, he found that the neutral or alkaline saliva, containing gastric juice secreted in the fasting state, very rapidly converted boiled starch into sugar, which did not undergo a further change into lactic acid for many hours. Shortly after a meal it often happened that no sugar could be detected in the gastric contents, while sugar could be easily recognised in the same mixture some hours afterwards — a proof that even small quantities of saliva are not impeded in their action on starch by the presence of the gastric juice. Similar facts were observed *within the body*. When boiled starch was introduced through the fistulous opening into the stomach, it rapidly underwent a change into sugar, while crude starch remained unchanged in the stomach for an hour and a half.*

In all probability the conversion of starch into sugar con-

* Although Schröder has thus arrived at a conclusion apparently opposed to the opinion of Bidder and Schmidt, it is but an act of justice to those most admirable experimenters to state that he made similar observations on a dog

tinues in the stomach until some at present undetermined degree of acidity is presented by the gastric contents. By adopting this view the opposing views can be harmonised, and in support of it may be adduced an experiment recently made (1854) by Kölliker, who prepared a strong digestive fluid from a pig's stomach and hydrochloric acid, and mixed it with human saliva in different proportions. He found that on taking equal quantities of the two fluids, the action on a solution of starch altogether disappeared; that with one part of gastric juice and two of saliva, sugar was found in twenty minutes; while with one part of the former to three or four of the latter, sugar appeared in from five to ten minutes.

(146.) The saliva exerts no definite metamorphic action on any of the carbo-hydrates, except starch; cane-sugar, gum, vegetable mucus (bassorin), and cellulose, remain unchanged in it; nor does it exert any chemical action on the protein-bodies or on gelatin, its utmost effect being to relax their tissues like pure water, and thus to render them more accessible to the action of the special secretion prepared for their transformation, the gastric juice.

Saliva in rabies.

(147.) There is one additional point in connection with the chemistry of the saliva which should be noticed, namely, the intensely poisonous character which it assumes in rabies. Our knowledge on this point is altogether negative. That the active agent in these cases is the sulphocyanide of potassium, which is assumed to be increased in rabies, is improbable, because this salt has been given to dogs in large doses without producing any decided poisonous effects; and, as it was rediscovered in the urine, it must have passed unchanged through the blood. An analysis of the secretions of the poison-glands of some of the venomous serpents might possibly throw some light on this subject.

with a gastric fistula, and, like them, he could find no sugar in the contents of the stomach. This discrepancy is probably due to the fact that the action of the dog's saliva on starch is much less rapid than that of human saliva, often not showing itself for ten or fifteen hours.

## SECTION II. — THE GASTRIC JUICE.

Gastric juice.

(148.) The chemical and physiological characters of the human gastric juice have been recently studied by Schmidt * and two of his pupils, Gruenewaldt † and Schroeder, under peculiar advantages. Their observations were conducted on an Esthonian peasant, Catherine Kütt, aged 35 years, and weighing about 118 lbs., in whom there had existed for three years a gastric fistula, three or four lines in diameter, under the left mammary gland, between the cartilages of the ninth and tenth ribs. The introduction of dry pease and a little water into the stomach through the opening occasioned (even in the morning, on an empty stomach) the secretion of from five to seven ounces of a clear limpid fluid with an acid reaction, which, however, was much less strong than Schmidt had observed in previous experiments on the gastric juice of dogs or sheep, in which he had established fistulous openings. It flowed through an elastic tube that was inserted into the fistula, sometimes in a thin stream, and sometimes in a rapid succession of drops.

Mode of obtaining it.

Its physical and chemical characters.

(149.) The acid and limpid fluid thus obtained was devoid of odour, had a mawkish taste, became very slightly turbid on the application of heat, and left, on evaporation, a yellowish brown, very acid, deliquescent residue, which, on incineration, yielded a colourless, neutral, or slight alkaline ash, that did not effervesce on the addition of acids. The density of the fluid varied from 1·0022 to 1·0024.

On examining the gastric juice under the microscope we find that it presents few morphotic elements; those which

* Schmidt, Ueber die Constitution des menschlichen Magensaftes, in Ann. d. Ch. u. Pharm., 1854, vol. xcii. p. 42.

† Gruenewaldt et Schroeder, Disquisitiones de Succo Gastrico Humano ope fistulæ stomachalis institutæ. Dorp. Liv. 1853.

are present consist partly of cells from the gastric glands, partly of their nuclei, and partly of finely comminuted molecular matter.

The following table gives the mean of two analyses * of the gastric juice of Catharine Kütt, with corresponding mean results of analyses of the same fluid in the sheep and the dog: —

| | Human Gastric Juice. | Sheep's do. | Dog's do. |
|---|---|---|---|
| Water . . . . . | 994·404 | 986·147 | 971·171 |
| Solid constituents . . | 5·596 | 13·853 | 28·829 |
| Ferment with a trace of ammonia . . . | 3·195 | 4·202 | 17·507 |
| Hydrochloric acid . . | 0·200 | 1·557 | 2·703 |
| Chloride of calcium . | 0·061 | 0·114 | 1·661 |
| Chloride of sodium . | 1·465 | 4·369 | 3·147 |
| Chloride of potassium . | 0·550 | 1·518 | 1·073 |
| Phosphates of lime, magnesia, and iron . . | 0·125 | 2·090 | 2·738 |

The fluid in the above analyses (all of which were made by Schmidt) cannot be regarded as perfectly pure gastric juice, because it contains the swallowed saliva. The chief effect of this admixture seems to be to diminish the quantity of free hydrochloric acid and to increase the phosphates.†

Its essential elements.

The gastric juice contains two essential elements — a free acid and a highly nitrogenous matter allied to the albumi-

* The analyses in this table were made by Schmidt himself with the gastric juice obtained in the manner above indicated. They differ very considerably from the analyses given in Gruenewaldt's Thesis (and which are to be found in my Appendix to Lehmann's Physiological Chemistry, vol. iii. p. 504.), in consequence of the different modes in which the fluids were obtained. In the latter case, the analysed fluid was the filtered contents of the stomach, shortly after a meal, which explains the large amount of solid residue.

† In corroboration of this statement, I may refer to the comparative analyses, instituted by Schmidt, of the gastric juice of dogs in their ordinary state, and with their salivary ducts tied. See "The Chemistry of Digestion," in the British and Foreign Medico-Chir. Rev., 1853, vol. xii. p. 184.

nates commonly known as *pepsin*, but to which Schmidt and his school have given the name of *ferment substance*. There is a great diversity of opinion regarding both these substances, and I shall briefly notice the most important views that have been brought forward regarding them.

Its free acid.

(150.) Prout (in 1824) maintained that the free acid of the gastric juice was hydrochloric acid, and Tiedemann and Gmelin, and several other writers, have adopted his view. Lehmann, on the other hand, asserts that lactic acid (either alone or associated with hydrochloric acid) is the main acidifying agent, and his experiments have been repeated and distinctly confirmed by Heintz, and are more or less supported by the observations of Bernard and Barreswil, Pelouze, R. D. Thomson, and others.* Blondlot again maintains that the acid reaction of the gastric juice is solely due to the presence of acid phosphate of lime — an opinion utterly at variance with the results obtained by all trustworthy chemists, and not deserving further notice. The most correct view seems to be that hydrochloric acid is always present, commonly but not always associated with lactic acid. In the gastric juice of the woman above referred to, Schmidt, in one analysis, found 0·022, and in another 0·018% of free hydrochloric acid and no lactic acid; while, in six analyses of the gastric juice of dogs, Lehmann found the free hydrochloric acid to range from 0·098 to 0·132%, and the free lactic acid from 0·320 to 0·585%.

When gastric juice is obtained for examination shortly after food has been taken, it is generally found to contain no free hydrochloric acid, but other free acids derived from the

* Alexis St. Martin, whose name is indelibly connected with the physiology of digestion through Dr. Beaumont's experiments, has again (1856) submitted himself to scientific observation. The acidity of his gastric juice has been studied by Professor R. E. Rogers, who finds that the main agent in producing the acid reaction is lactic acid, and that if hydrochloric acid be present, it is only in very small quantity.

decomposition of the food, especially lactic and butyric acids.

(151.) Our knowledge of pepsin is still very imperfect. It is closely allied to the protein-bodies, does not coagulate when heated, but is deprived by that process of its characteristic property of dissolving the protein-bodies and of converting them into the non-coagulable substances, to which Lehmann has given the name of *peptones*. It is precipitated by corrosive sublimate, the salts of lead, alcohol, and tannic acid. It may be separated from the mercury and lead compounds by sulphuretted hydrogen, and, on the addition of a few drops of dilute hydrochloric acid, possesses a great solvent power over coagulated albumen. Schmidt, some years ago, suggested and still adheres to the view that the active principle of the gastric juice should be regarded as a compound of pepsin (or as he terms it, ferment or ferment-substance) and hydrochloric acid—in short, as a conjugated acid whose negative constituent is hydrochloric acid with coagulated pepsin as an adjunct. He regards it as more nearly resembling lignosulphuric acid than any other conjugated acid, and as this becomes disintegrated into dextrine and sulphuric acid, so the *pepsin-hydrochloric acid* becomes separated at 212° into coagulated pepsin and hydrochloric acid; and in either case it is equally impossible to reproduce the compound from the separated proximate principles. It is unnecessary to enter further into this view because, ingenious as it is, and singularly as it seems to harmonise with certain facts, there are other and very important facts which render its correctness doubtful. Thus, for instance, the existence of the pepsin-hydrochloric acid has not been established by any analysis of a combination of it with a mineral base or with an albuminous substance; and Lehmann, who has instituted numerous experiments regarding the quantitative relations between the digestive fluid and the substances to be digested, states that he cannot ascertain that there are any such proportions between the acid and the

Pepsin.

digested substance as at all accord with the ordinary acid or basic combinations of acid and base.

Besides pepsin, the gastric juice contains another more soluble organic matter, which has not been accurately studied.

Mineral constituents.

(152.) The mineral constituents of the gastric juice consist chiefly of chlorides, as may be seen by a glance at the analyses in page 159. In addition to an abundance of chloride of sodium we have smaller quantities of the chlorides of ammonium, calcium, and magnesium, with traces of the phosphates of lime, magnesia, and iron.

Abnormal constituents.

(153.) Very little is known regarding the abnormal constituents which, under certain conditions, may occur in the gastric juice. In gastric catarrh we may have an excess of mucus, which sometimes, even while in the stomach, may undergo decomposition, and, on coming in contact with amylaceous or saccharine food, may establish acetic, butyric, or lactic fermentation, in which case the contents of the stomach contain far more free acid than occurs in them in normal digestion. Urea has often been found in vomited matters in cases of uræmia, consequent on Bright's disease or on cholera. Lehmann, however, states that in these cases he has always found the contents of the stomach and the vomited matters strongly alkaline and always rich in carbonate of ammonia, but never containing urea.

Quantity of the gastric juice.

(154.) The quantity of gastric juice secreted in twenty-four hours was determined by Bidder and Schmidt in the case of sheep to be one-eighth, and in that of dogs to be about one-tenth of the whole weight of the body. Assuming the latter ratio to be true for men, a man of ordinary weight, say of ten stone, would secrete about fourteen pounds of this fluid. In the case of Catherine Kütt the mean daily quantity amounted to no less than fourteen kilogrammes, or about thirty-one pounds, that is to say, to more than a fourth part of the weight of the body. On this calculation a man of ten stone would daily secrete thirty-seven pounds of gastric juice. As

might naturally be expected, the quantity and the density of the gastric juice in these cases stand in an inverse ratio to one another.

(155.) There is no ambiguity regarding the function of the gastric juice. It serves not only to dissolve but also to modify the nitrogenous elements of the food (the protein-compounds and their derivatives), converting them into thoroughly new substances (peptones), which, although they coincide in their chemical composition and in many of their physical properties with the substances from which they are derived, essentially differ from them, not only in their ready solubility in water and even in dilute spirit, but in having now lost the faculty of forming insoluble combinations with most metallic salts. The formation of these peptones depends solely on the action of the gastric juice, and occurs without the evolution or absorption of any gas, and without the production of any secondary substance. Its function.

This power is suspended by boiling the gastric juice, by saturating its free acid with an alkali, by sulphurous and arsenious acids, by alum, and by most metallic salts; and it is very much impeded by the addition of alkali-salts, and by saturating the fluid with soluble organic compounds. The addition of water to a gastric juice which has been already saturated by a peptone, enables it to resume its digestive powers, which are also restored, to a certain degree, by the addition of free lactic or hydrochloric acid.

Fats, when added in certain quantity to the gastric juice, promote the conversion of the protein-bodies into peptones.

Bidder and Schmidt found, in the course of their numerous experiments, that gastric juice mixed with saliva had a less energetic digestive power than pure gastric juice obtained from animals whose salivary ducts were tied—a fact obviously dependent on a portion of the free acid being saturated by the alkaline saliva. They likewise found that the addition of bile to the gastric juice entirely suspended its solvent action;

although the mixture still remained decidedly acid. The latter fact demonstrates that, when undigested albuminous matters pass into the intestine, the gastric juice must lose all power over them.

According to Lehmann's experiments, 100 grammes of fresh gastric juice are capable of dissolving 5 grammes of coagulated albumen.*

All our best observers agree that the gastric juice exerts no apparent action on the non-nitrogenous articles of food, namely, the fats and carbohydrates.† As the fats unquestionably exert a favourable influence on the digestion of nitrogenous matters, it is probable that they undergo some slight change, but the quantity of fatty matter which is modified during the digestive process is so minute as not to be appreciable by analysis. Starch, gum, and sugar, when placed in pure gastric juice at the temperature of the animal body, do not undergo any change corresponding to true digestion.

Insufficient for the digestion of all the nitrogenous food.

(156.) Although the main object of the gastric juice is to dissolve the protein-bodies, it does not suffice to dissolve the quantity necessary for the proper nutrition of the organism. Since a dog secretes about 100 grammes of gastric juice for every 1000 grammes of its bodily weight (10%), it would only be

* Schmidt, who instituted numerous experiments of a similar kind, arrived at a far lower result. He found that on an average 100 grammes of the gastric juice of the dog dissolved only 2·2 grammes of coagulated albumen — rather less than half the quantity obtained by Lehmann. It is probable that the higher number obtained by the last-named chemist was due to the presence of lactic acid which did not exist in the gastric juice used by Schmidt. Since many conditions favouring digestion co-operate within the stomach, and since the gastric juice obtained from dogs with fistulous openings may possess less digestive power than that which is secreted from uninjured stomachs, Schmidt believes that the gastric juice may be able to dissolve a larger amount of albuminous matter than these results would seem to indicate.

† Professor R. E. Rogers, of the Pennsylvania University, who has been recently (1856) examining the chemical relations of the gastric juice obtained from Alexis St. Martin, arrives, however, at the startling conclusion, that "the conversion of starch into grape-sugar may take place in the stomach independently of the action of saliva"!

able (taking Lehmann's estimate, which is more than twice as high as Schmidt's) to digest 5 grammes of dry or coagulated albumen for that amount of weight; but a dog, in order to keep in condition on an exclusive flesh-diet, (and this is its natural food,) should take 50 grammes of flesh, containing 10 grammes of dry albuminates, for every 1000 grammes of weight. Hence its gastric juice only suffices for the digestion of half the albuminates necessary for its nutrition — a result which will be fully explained when we treat of the intestinal juice, and which is quite in accordance with the observed fact, that a considerable portion of the albuminates enters the small intestine in an undissolved state. On comparing the experiments made by Hübbenet on dogs with those made by Schroeder on Catherine Kütt, we have evidence that in man the gastric digestion of the albuminates must be more imperfect than even in the dog; for, while in the latter 46·8% and 77·1% of coagulated albumen were dissolved in four and six hours respectively, only 23·6% and 39·1% were dissolved in five and eight hours respectively in the human stomach: and similarly, raw flesh introduced in small muslin bags into the human stomach did not become entirely dissolved for nineteen or twenty hours, while in the dog the same process did not occupy more than from two and a half to four hours.

Why the stomach is not itself digested.

(157.) The vitality of the stomach has been usually assigned as the reason why it is not digested by its own secretion. Recent observations of Bernard*, confirmed in this country by Dr. Pavy, show, however, that mere vital force can offer no available resistance to the chemical force of the gastric juice. On inserting the hind legs of a live frog into a dog's stomach, through a fistulous opening, the flesh of the extremities is almost as rapidly dissolved as if it did not belong to a living animal. The resisting power of the stomach seems due to the continuous re-formation of epithelium during the process of digestion.

* Leçons de Physiologie Expérimentale, 1856, vol. 2. p. 408.

## SECTION III. — THE BILE.

Its general properties.

(158.) The bile of most mammals, as obtained from the gall-bladder, presents the following properties in common. It is a viscid and tenacious fluid of a green or brown colour, with a bitter taste and (especially on the application of warmth) a peculiar and often musk-like odour. Its specific gravity is about 1·020; it is usually faintly alkaline, but often perfectly neutral. Bile in its ordinary state putrefies very readily, but after it is freed from mucus, it altogether ceases to exhibit that tendency.

Fresh human bile can only be obtained from the bodies of criminals who have been executed, and has been very rarely examined. Most of our knowledge regarding the biliary secretion and the influence of bile on the digestive system has been derived from observations on animals, in which the bile-ducts were tied and biliary fistulæ had been established.

Its chemical constituents.

(159.) The bile, in the case of all animals, contains two essential constituents, one of which is of a resinous nature while the other is a pigment.

The resinous constituent is not precisely identical in all kinds of bile; it generally consists of a soda-salt whose acid is one of the conjugated acids, with glycine or taurine as its adjunct, described in pp. 60-61. Strecker, to whom we are mainly indebted for our knowledge of the chemistry of the bile, states that in most mammals the resinous constituent merely differs in the varying proportions in which the taurocholates and glycocholates are intermixed, the taurocholates usually preponderating. The bile of the dog consists almost exclusively of taurocholate of soda. The bile of the pig presents certain chemical peculiarities, one of which is noticed in § 53.

The only bird whose bile has yet been analysed is the

goose. Taurocholates are present in the secretion to the almost entire exclusion of glycocholates.

The same is the case with the bile of fishes (the cod, pike, &c.), in which the resinous constituent consists of taurocholates, with mere traces of glycocholates. It is worthy of notice that, contrary to what might have been expected, potash-salts preponderate in the bile of sea fishes, and soda-salts in that of fresh-water fishes.

In most kinds of bile the resinous constituent amounts, according to Lehmann*, to at least 75% of the solid residue, but this seems too high an estimate.

Bile pigment.

The bile-pigment occurs in the bile of different animals under two forms, namely, as a brown and as a green pigment, the latter most probably, however, being a product of the oxidation of the former. The normal quantity of pigment in the bile has not been determined.

Cholesterin.

Another constituent that is invariably present in the bile is cholesterin, which is probably held in solution by the taurocholate of soda, since it very rarely occurs in the bile in a crystalline form. It occurs in extremely small quantity.

Free fats, which are also held in solution by the taurocholate of soda, and saponified fats, are ordinary constituents of bile, and with the cholesterin formed, in Gorup-Besanez's two cases, 27 and 30% of the solid residue.

As the taurocholic and glycocholic acids, the fatty acids, and, as we shall presently see, the pigment, are combined with alkalies or alkaline earths, it is obvious that the process of incineration will completely modify all pre-existing relations amongst the inorganic constituents. The only trustworthy analysis of the mineral constituents of the bile is that of

* Lehmann deduces this number from a knowledge of the quantity of sulphur in the bile, as determined by Strecker, Bensch, and others. All the sulphur is contained in the taurine, and every 100 parts of taurocholate of soda contain 6 of sulphur. The numbers actually obtained by Gorup-Besanez from the bile of two criminals immediately after their execution were considerably lower, namely 55·4 and 60·8%.

Weidenbusch *, who found in ox-bile chloride of sodium in large quantity (27·7%), tribasic phosphates of soda and potash, carbonate of soda, phosphates of lime and magnesia, and small quantities of iron, manganese, and silica.

Mucus.

Finally, the bile always contains a certain amount of mucus secreted by the lining membrane of the gall-bladder. It is to this constituent that the bile mainly owes its viscid property. The cylinder epithelium contained in this mucus is the only morphotic element in fresh normal bile.

Amount of solid constituents.

Human bile contains, according to Frerichs, 14% (or rather less) of solid constituents, while in the two cases analysed by Gorup-Besanez, it yielded 10·19 and 17·73% respectively. The bile of the ox yields from 10 to 13%, and that of the pig from 10·6 to 11·8%.

The organic constituents of human bile collectively amount to about 90%, Frerichs fixing them at 87, and Gorup-Besanez at 93·6%, while the organic constituents of the bile of most mammals are rather less abundant, namely about 87%.

Difference between cystic and hepatic bile.

(160.) We are indebted to the researches of Bidder and Schmidt for almost all the knowledge we possess regarding the differences between fresh hepatic and cystic bile. The fresh bile of carnivorous animals (dogs, cats, crows) is yellow or yellowish brown, while that of herbivorous animals (rabbits, sheep, geese) is green. The colour of cystic bile in the former class of animals, is for about three hours after a meal as yellow as the hepatic bile, but it then becomes greenish, and if no food has been taken for twenty hours it assumes a deep green tint. As hepatic bile gradually becomes green on exposure to the atmosphere, and as, further, the yellow tint re-appears on the application of deoxidising agents, we cannot entertain a doubt that this change of colour is dependent on an oxidation effected by the arterial blood in the capillaries of the inner coat of the gall-bladder

* Pogg. Ann. 1849, vol. 76. p. 386.

Prolonged retention of the bile in the gall-bladder gives rise to a very decided concentration of that fluid. Thus, while the fresh hepatic bile of dogs and cats contains, on an average, 5% of solid constituents, the cystic bile may contain from 10 to 20%, according to the length of its retention; and while the fresh bile of the rabbit contains only 2%, the cystic bile may yield as much as 15%. The bile of the goose and of the crow yielded similar results.

Abnormal constituents.

(161.) The most important abnormal constituents of the bile are albumen and urea. The former has been observed in cases of fatty liver and of Bright's disease, while the latter has been found in cases of uræmia, as, for instance, in Bright's disease and cholera — a result quite in accordance with an observation that had been previously made, namely, that urea occurs in the bile after the extirpation of the kidneys.

Bile which, in consequence of disease, has been retained for a long time in the gall-bladder, occasionally presents a sediment which, when examined under the microscope, is found to consist of greenish or brownish rod-like molecules, or of crystals arranged in rows. The term *bilifulvin* has been applied by Virchow to the substance forming these sediments, and we occasionally find intermingled with these molecules those crystals of hæmatoidin which are also found in old extravasated blood.

We possess very little accurate knowledge regarding the changes which the bile undergoes in disease. It appears to be abnormally watery after severe inflammations, especially in cases of death from pneumonia; and a similar change seems to be impressed upon it by dropsies, diabetes, typhus, and occasionally by tuberculosis; while there is an excess of solid constituents in diseases impeding the venous circulation in the abdomen, and in cholera. The mucus is sometimes extraordinarily increased, especially in cases of typhus.

Gall-stones.

(162.) In connection with the morbid conditions of the

biliary secretion we must notice *gall-stones.** There are several varieties of these concretions. We may have a nucleus consisting of a chemical compound of pigment and lime, pigment-lime as it may be termed for brevity (first described and shown to be a frequent cause of the formation of gall-stones by Bransom)†, while the bulk of the stone is made up of cholesterin; or the pigment-lime and cholesterin may be more uniformly diffused through the concretion; or if the gall-stone be of a blackish or dark green colour it probably consists of the pigment in a modified state, but still in combination with lime: in such concretions as these there is usually little or no cholesterin.

Biliary concretions in which carbonate and phosphate of lime are the chief ingredients are very rare.

Quantity of bile.

(163.) We have never had an opportunity of directly observing the quantity of bile that is secreted in the human subject, and it is extremely improbable that we shall ever have a case presenting the two conditions of a thoroughly closed *ductus communis* and a fistulous opening connected with the gall-bladder. All our information on the amount of the daily secretion of bile is derived from observations on animals in which these conditions have been artificially induced.

Bidder and Schmidt‡ found from numerous experiments and observations that there was secreted, for 1000 grammes' weight of the animal,

| | In the Cat. | Dog. | Sheep. | Rabbit. | Goose. | Crow. |
|---|---|---|---|---|---|---|
| Fresh bile . . . | 14·500 | 19·990 | 25·416 | 136·84 | 11·784 | 72·096 |
| Solid constituents. | 0·816 | 0·988 | 1·344 | 2·47 | 0·816 | 5·256 |

* The general history of gall-stones is very ably discussed in Vogel's "Pathological Anatomy of the Human Body," 1847, pp. 369—375. On this subject, and, indeed, on animal concretions generally, I may refer the reader to a recent work by von Hemsbach (published after his death by Billroth) entitled "Mikrogeologie. Ueber die Concremente im thierischen Organismus." Berlin, 1856.

† Zeitschr f. rat. Med. 1846, vol. 4. pp. 193—208.

‡ Op. cit.

Similar observations have been subsequently made on the dog by Nasse, Arnold, and Kölliker and Müller.* The last named physiologists have arranged in a tabular form the results of all the observations made on the daily amount of bile secreted by the dog. The conclusion at which they arrive from their own experiments is that a dog for 1000 grammes' weight secretes daily 36·1 grammes of bile containing 1·162 grammes of solid residue. If the same proportion holds good for the human species, a man weighing ten stone would daily secrete 2310 grammes or about five pounds of bile.

Agents influencing the quantity of bile

(164.) Although there is a continuous secretion of bile, equal quantities are not secreted in equal times. The experiments instituted during the last few years by Bidder and Schmidt, Arnold, and Kölliker and Müller, show that the flow of bile is considerably modified by the digestive process. Their results are, however, somewhat discordant. According to Bidder and Schmidt the secretion (in dogs) is most abundant in from thirteen to fifteen hours after feeding, while Arnold found that the secretion was most copious at a more early period and that it began to decrease from the fourth hour. Kölliker and Müller find that in the first and second hour after a meal very little bile is secreted — less even than in the nineteenth and subsequent hours. In the third, fourth, and fifth hours there was, with scarcely an exception, an augmentation of the secretion; indeed, in a few cases it reached its maximum in the fifth hour, while in all the others this was attained in the sixth, seventh, or eighth hour, after which the quantity gradually diminished, but the minimum was reached in from the nineteenth to the twenty-fifth hour. There seems reason for believing that the period at which the maximum secretion takes place is dependent on the amount of the meal. After a moderate meal it occurred between the

* Verhandl. d. phys.-med. Gesellsch. in Würzburg, 1856, vol. 7. p. 464.

fifth and eighth hours, as in Kölliker and Müller's observations, while after a very copious repast it is retarded, as in Bidder and Schmidt's experiments. This is Kölliker's explanation, and some of his own facts are confirmatory of its accuracy.

Bidder and Schmidt have ascertained that when animals are deprived of food for a longer period than twenty-four hours (as, for instance, two, three, seven, or ten days) the biliary secretion continuously decreases. Thus, for instance, in cats the quantity of bile secreted on the tenth day did not exceed the fourth part of what they secreted during the twenty-four hours immediately succeeding a meal.

All observers concur in the view that the amount of the biliary secretion varies directly with the quantity of the food; and as animals with biliary fistulæ usually have voracious appetites, experiments on this point are easily made. Kölliker and Müller found that on increasing a dog's food 56% they caused an augmentation of the bile amounting to 58%, and its collective solid constituents were increased in a similar ratio.

Moreover, the nature of the food probably exerts a certain influence on the amount of the biliary secretion. A flesh-diet appears, according to numerous experiments, to cause a more abundant secretion of bile than vegetable food; but as the results on this point are contradictory, no great weight can be attached to this influence.

The addition of fat to the ordinary flesh-diet of a dog causes a considerable augmentation of the biliary secretion (Nasse), but on an exclusive fat-diet animals secrete no more bile than if they were actually starving.

Copious water-drinking increases the quantity of bile, and not merely of its water but of its solid constituents.

Carbonate of soda in large doses occasions a considerable diminution in the amount of bile, while calomel increases the watery portion but not the solid constituents of the bile.

Both Nasse and Bidder and Schmidt found that the quan-

tity of bile was considerably diminished when the animals on which they experimented presented any febrile symptoms.

Functions of the bile.

(165.) Numerous and often opposite views have at different times been advanced regarding the functions of the bile.

The view that the secretion of the bile is mainly for the purpose of purifying the blood — of removing from it the carbonaceous matters not separated by the lungs — is opposed by the following considerations: — first, there is no evidence that the quantity of bile is increased when the process of oxidation in the lungs happens to be impeded; secondly, pathological anatomy yields us no facts in favour of the view that the liver can act vicariously for the lungs; and, thirdly, the separation of carbon by the liver is so inconsiderable as compared with that by the lungs (being at most one-tenth, and sometimes only one-fortieth according to Bidder and Schmidt), that the liver can hardly be regarded as a purifier of the blood in so far as the carbon is concerned.

The bile probably co-operates in more ways than one in the general process of digestion.

One use that has been ascribed to it is to neutralise in the small intestine the acid chyme which emerges from the stomach. But the bile can contribute little or nothing to the neutralisation of the free acid, because in the first place the bile is very slightly alkaline and often perfectly neutral, and, secondly, because the chyme in the intestine is still acid after the admixture of the bile. The following reaction probably takes place: — the alkali of the bile leaves the resinous and fatty acids, with which it was combined in the bile, and unites with the stronger acids of the chyme, namely, hydrochloric and lactic acids; the biliary acids thus liberated give an acid reaction to the chyme until they become decomposed.

The bile has also been asserted to possess a special solvent action on the chyme, but none of its ordinary constituents seem to be essentially changed, even when digested for a long time with fresh bile; and the only effect of this nature that is

actually produced is probably due to the large quantity of water in the biliary secretion.

It is doubtful how much importance should be attached to the antiseptic action of the bile on the contents of the intestinal canal. In favour of such a view it is alleged that when no bile is poured into the intestine its contents very soon undergo putrefactive decomposition — a circumstance that is sometimes observed in patients with jaundice, and which was noticed by Frerichs in animals after tying the ductus choledochus. On the other hand, other experimentalists have found that animals, thus operated on, lived and discharged normal excrements for many months.

Another use that has been assigned to the bile is that it exerts a stimulating action on the intestinal walls, and thus acts as a normal purgative.

But the main use of the bile seems to be to promote the digestion of fatty matters. The bile possesses so small a solvent action on the fats that the whole quantity which is secreted would be quite insufficient to dissolve the amount of fatty matter which is known to be absorbed by the intestines; but this secretion seems to exert a peculiar physical action on the fat and on the intestinal walls, disintegrating the former and impressing on the latter (by moistening the villi) a peculiar condition which singularly facilitates the absorption of fatty matters. This view is confirmed both by direct experiments out of the body, and by observing the phenomena that occur when the flow of bile into the intestine is prevented. (1.) Wistinghausen* has shown by a series of accu-

* A tolerably full report of his inaugural dissertation, entitled "Endosmotic Experiments on the Action of Bile on the Absorption of the Neutral Fats," is given in Schmidt's "Jahrbücher," 1852, vol. 75. p. 148. Instead of actual bile he employed a solution of mixed glycocholate and taurocholate of soda (5%). In a tube moistened with this fluid, oil rose 6·3 times higher than in a corresponding tube moistened with water; and when a mixture of 5 parts of this solution, 1 of albumen and 1 of a solution of potash (1%) was used, the oil rose eight times higher. Bidder and Schmidt seem to have used actual bile in their own experiments. Op. cit. p. 231.

rate observations (conducted under Schmidt's superintendence) that oil will rise many times higher in a capillary tube moistened with bile than in a similar tube when dry or when moistened either with pure water or with a saline solution, and similarly that it passes through membranes saturated with bile far more readily than through similar membranes moistened with water. (2.) It is found that those animals in which the ductus choledochus has been tied, and whose bile escapes externally through a fistulous opening, digest the same quantities of albuminous and amylaceous food as similar animals in a normal state; but the case is very different when the quantities of fat are compared with one another which are retained in the body and applied to the purposes of life by the animals that had been operated on and by healthy animals. It has been clearly shown by Bidder and Schmidt's experiments on dogs and cats, in which the fatty matter in the food and in the excrements was compared, that, although a certain quantity of fat is absorbed independently of the action of bile, at least 2·5 times more is absorbed in conjunction with the biliary secretion.*

In order to determine in another manner the influence of the bile on the absorption of fat, the amount of fat in the chyle obtained from the thoracic duct of healthy dogs, fed on fat, was contrasted with that obtained from the corresponding fluid obtained from dogs in which the bile did not flow into the intestine. In two dogs with biliary fistulæ the chyle yielded 0·834% of fatty acids mixed with other organic matters, and 0·113% of fatty acids with 0·190% of free fat respectively, while the chyle of a healthy dog that eight hours before its death had been fed upon raw beef, contained 3·244% of free fat with 0·058% of fatty acids.†

* In other experiments they found that five and even seven times more fat was absorbed when the bile flowed freely into the intestine than when it was excluded. Op. cit. p. 224.

† If instead of taking the percentage in relation to the whole chyle we take the percentage of the fat (including under this term both the free fat and the

These experiments afford a complete demonstration of the importance of the bile in relation to the absorption of fat, and explain the mode in which it acts.

Schlossberger has lately suggested the probability that certain fatty matters occurring in the brain and nerves (cerebric acid, oleophosphoric acid, &c.) take their origin from some of the biliary constituents. We shall return to this subject in Chapter XVI. in the Section on the "Composition of the Brain and Nerves."

Formation of bile.

(166.) It may now be regarded as an established fact that the bile is actually formed in the liver, and that it is not merely separated from the blood by that gland. This view is established beyond all question by the following observations: —

1. Several physiologists (amongst whom Moleschott should be especially mentioned) have extirpated the livers of frogs, and succeeded in keeping the mutilated animals alive for some days. Neither the blood, lymph, flesh, nor urine of these frogs yielded the slightest traces either of the resinous acids or of the pigment of the bile.

2. Jaundice very seldom occurs in diseases of the parenchyma of the liver (almost never in fatty degeneration and in tuberculosis of that organ, and very rarely in simple atrophy, in granular liver, and in hepatitis), while it is almost constantly present in diseases of the biliary ducts: if an accumulation of biliary matters were induced in the blood by the suppression of the hepatic secretion, jaundice would occur just as frequently in the first class of diseases as in those which present a mechanical impediment to the excretion of the bile.

3. None of the essential constituents of the bile can be detected in the portal blood.

fatty acids) in the solid residue, the numbers are 14·3%, 5·4%, and 39·5%. The analyses of the chyle are given in pp. 226-227. of Schmidt's book: they do not differ from one another materially except in reference to the fats.

We have already shown in § 28. that there are strong reasons for believing that the non-nitrogenous resinous acid of the bile (cholic acid) is formed from the oleic acid (or olein) of the portal blood; and this view is supported by the fact that the amount of fat which is conveyed to the liver by the portal vein is far greater than that which leaves it by the hepatic veins, as well as by various arguments already given in p. 80.

How and where its adjuncts, taurine and glycine, are formed is a more doubtful point. Taking into consideration the facts mentioned in p. 31. regarding the modes in which glycine is artificially obtained, and the evidence afforded by recent researches (see p. 53.) regarding the occurrence of taurine in the muscles of certain of the lower animals and in the lungs and kidneys of mammals, little doubt can remain that these substances are products of the regressive metamorphosis of the nitrogenous tissues. Our tests for the detection of minute traces of these substances are not sufficiently delicate to enable us to state authoritatively that they must be formed in the liver *because* we cannot discover their presence in the portal blood. But there are other grounds which render it most probable that their formation takes place in the liver. These are (in the case of taurine):—(1.) That there is considerably more sulphur in the solid residue of portal blood than in that of the blood of the hepatic veins (the ratio being, in Lehmann's analyses, as 0·393% to 0·331%), and it is very probable that this excess of sulphur (whether derived from the disintegration of the fibrin which takes place in the conversion of portal into hepatic venous blood, as shown in § 216, or from an unknown sulphur-compound which Lehmann detected in the spirit-extract of portal blood) is applied to the formation of taurine; and (in the case both of taurine and glycine) (2.) that it is the ordinary chemical rule (and only few exceptions are known) that conjugated compounds, such as taurocholic and glycocholic acids, are not directly formed from the two bodies into which they become separated on decomposition: chemical

experience, therefore, renders it improbable that these conjugated acids should be formed from pre-existing taurine or glycine and cholic acid; and to this argument we may add that there is an additional improbability in supposing that in the regressive metamorphosis of tissues two comparatively simple substances should combine to form much more complicated ones.

We have already noticed the different views that have been advocated regarding the formation of the bile-pigment in p. 97.

## SECTION IV. — THE PANCREATIC FLUID.

Pancreatic fluid; its general properties.

(167.) The pancreatic fluid, as obtained from a well-healed permanent fistula, is a colourless, clear, somewhat viscid and ropy fluid, of a mawkish alkaline taste, devoid of any special odour, and exhibiting a strong alkaline reaction.

Schmidt *, who has reinvestigated the chemical characters of this fluid since the publication in 1852 of his great work on "The Digestive Fluids," ascribes to it the following properties: — Its specific gravity is 1·010 or 1·011, it froths extremely on being shaken, instantaneously converts boiled starch into dextrine and sugar at about 100° F., becomes turbid at 158°, and coagulates in white flakes at 162°. It is also coagulated by alcohol, the coagulum (pancreatic diastase) redissolving in pure water and retaining its power of metamorphosing starch. By raising the pancreatic juice to the boiling point this power is, however, destroyed, as also by the addition of sulphuric, hydrochloric, nitric, and metaphosphoric acids, and by corrosive sublimate, which form abundant white precipitates; while acetic, sulphurous, and tribasic phosphoric acids, potash, and ammonia, if added to the extent merely of a few drops, suspend the metamorphic action without inducing even any turbidity. The two last-named

* Ann. d. Ch. u. Pharm. 1854, vol. xcii. p. 33.

alkalies, as well as carbonate of ammonia, prevent the coagulation by heat. Neutral acetate of lead produces a thick white flocculent precipitate which partially redissolves in an excess of the test; both the precipitate and the solution act on starch. This property of the pancreatic juice is, moreover, in no way affected by the addition of bile or of gastric juice. It has no power of establishing fermentation in saccharine fluids or of converting urea into carbonate of ammonia.

This secretion is so prone to decomposition that after exposure to the air for a few hours it developes a distinct odour of putrefaction.

Its chemical composition.

(168.) The principal constituent of the pancreatic juice is a substance closely resembling but not perfectly identical with albuminate of soda; it is the pancreatic diastase or ferment to which allusion has already been made. It is to this substance that the pancreatic juice mainly owes its principal chemical and physiological properties. The quantity in which it occurs may be seen by a glance at the analyses given below.

Amongst the other organic constituents we may mention a butter-like fat which was found in small quantity (0·026%) by Frerichs in the pancreatic juice of the ass, and leucine and tyrosine, which were detected in minute proportions by Kölliker and Müller.* No trace of sulphocyanides has ever been found in this secretion.

The mineral constituents consist chiefly of the chlorides of sodium and potassium, and of the phosphates of the alkalies and earths.

In the following table A. represents the mean of three analyses (made by Schmidt) of the pancreatic juice of dogs in which permanent fistulous openings had been established, while B. represents the composition of the same secretion immediately after the operation. The second analysis is

* Verhandl. d. phys.-med. Gesellsch. in Würzburg, 1856, vol. vi. p. 506.

given with the view of showing how much severe operations may modify the animal fluids.

| | A. | B. |
|---|---|---|
| Water . . . . . | 980·45 | 900·76 |
| Solid constituents . . . . . | 19·55 | 99·24 |
| Pancreatic diastase or ferment . | 12·71 | 90·44 |
| Inorganic bases and salts . . . | 6·84 | 8·80 |
| Soda combined with the ferment | 3·31 | 0·58 |
| Chloride of sodium . . . | 2·50 | 7·35 |
| Chloride of potassium . . . | 0·93 | 0·02 |
| Phosphate of lime . . . . | 0·07 | 0·41 |
| Phosphate of magnesia with traces of oxide of iron . . | 0·01 | 0·12 |
| Tribasic phosphate of soda . . | 0·01 | — |
| Lime and magnesia combined with the ferment . . . | 0·01 | 0·32 |

The pancreatic juice yielded by dogs with permanent fistulous openings varied considerably in its composition; the collective solid constituents ranged from 1·5 to 2·3%; the organic matters from 0·9 to 1·6%, and the inorganic bases and salts from 0·62 to 0·75%.

Its daily quantity.

(169.) Calculating from the quantity of pancreatic juice secreted by dogs of known weight in a given time, Schmidt infers that a man weighing ten stones secretes daily 4·6 kilogrammes, or about 10 lbs. of this fluid.

Various circumstances modify the amount of the secretion: thus Ludwig and Weinmann found that prolonged hunger, vomiting, and severe operations (such as establishing fistulous openings) diminished the quantity, while it was increased by the ingestion of solid food or of fluids. The flow seemed to attain its maximum in twelve or thirteen minutes after water had been taken.

The following inferences are drawn by Kroeger from numerous observations: —

1. The ingestion of food exercises great influence over this secretion, the latter becoming much increased in quantity almost immediately after meals, and reaching its maximum in half an hour or three quarters after the meal, when it is six or ten times larger than it had been just before the ingestion of food.

2. Water does not produce a similar effect; on the contrary, when taken simultaneously with solid food, it prevents the latter from causing so evident an increase.

3. The concentration of the pancreatic juice is commonly, but not invariably, diminished in the same proportion as the quantity is increased.*

Its functions.

(170.) One of the chief uses of the pancreatic juice in relation to digestion is doubtless to convert into sugar the amylaceous matters which have escaped the action of the saliva and have passed unchanged into the duodenum. The pancreatic juice possesses this property in a far higher degree than the saliva, and this power is not impeded by an admixture of bile, gastric juice, or free acids. Comparative anatomy supports this view, which was established on purely chemical *data*, for the pancreas is found to be much more developed in herbivorous than in carnivorous animals.

Bernard claims for the pancreatic fluid another and apparently a more important function; he believes that he has proved that it is solely by the action of this fluid that the fat is reduced to a condition in which it can be absorbed and digested; that is to say, that it is decomposed into glycerine and a fatty acid. It is unquestionable that if pancreatic juice and fat be shaken together in a test tube an emulsion is immediately formed and the fat is in a short time decomposed into acid and base. But the experiments of Frerichs, Lenz, Bidder and Schmidt, and Lehmann seem to

* Diss. Inaug. de Succo Pancreatico, Dorpat, 1854, pp. 40, 41.

afford conclusive evidence that a similar result does not take place in the intestinal canal, and it is most probable that it is in consequence of its admixture with the acid gastric juice that the pancreatic fluid loses this property. In support of the view held by Bernard's opponents it may be further urged that the chyle always contains a far larger amount of the neutral fats than of fatty acids, and that after the establishment of a fistulous opening which allows of the external escape of the pancreatic fluid, the fat taken with the food seems to be absorbed as readily and completely as before the operation.*

Considering the large quantity of pancreatic juice yielded in the twenty-four hours (about 10 lbs.), Schmidt is of opinion that the function of this fluid is not so much to promote the conversion of starch into sugar as for the purpose of diluting the chyme, and for reconverting the soda (which in the pancreas has been separated from the chlorine of the chloride of sodium and has combined with organic matter) into chloride of sodium. According to this view he shows from numerical calculations that more than half of the chloride of sodium existing in the blood circulating through the pancreas, is broken up into hydrochloric acid and soda, of which the former is separated by the glands which secrete the gastric juice, while the latter unites with the pancreatic diastase or ferment. Meeting again in the upper part of the intestinal canal the hydrochloric acid and the soda re-unite and re-form chloride of sodium, which is again absorbed and re-enters the circulation.

We have already referred to the occurrence of leucine in the pancreatic fluid and in the saliva. It is possible that its decomposition may give rise to the volatile fatty acids which are occasionally found in the stomach and small intestine.†

* Bernard still maintains the accuracy of his views, and asserts that his opponents failed in confirming them from an imperfect anatomical knowledge of the parts on which they operated. See his "Leçons de Physiologie Experimentale," 1856, vol. ii. pp. 335 — 349.

† See note to page 32.

## SECTION V. — THE INTESTINAL JUICE.

(171.) The intestinal juice secreted by the glands of Lieberkühn and other glandular structures embedded in the mucous coat of the intestine is a colourless (or, according to Kölliker, yellowish), ropy, viscid fluid, which is invariably alkaline; the alkalinity, however, varies in different animals and in different parts of the intestine. The intestinal juice; its properties.

The morphotic elements occurring in the intestinal juice are a certain number of granular cells, nuclei, sometimes a few fat globules, and not unfrequently cylinder epithelium.

After the removal (by filtration) of these elements, the fluid (according to Schmidt) does not contain a trace of albumen, and, therefore, does not coagulate either on boiling or the addition of acetic acid; according to Kölliker, however, a couple of drops of acetic acid produce a turbidity in the heated (but not the cold) fluid, which disappears on the addition of an excess of the reagent. Acetate of lead, nitric acid, and alcohol throw down tolerably abundant precipitates. Its chemical composition.

In the following table A represents the composition of a filtered and B of an unfiltered specimen of the intestinal juice of the dog. The analyses were made by Schmidt.

A.

| | |
|---|---|
| Water . . . . . | 965·33 |
| Solid matters not volatile at 248° . . . . | 34·67 |
| Substances soluble in alcohol of 85% (bile and soluble salts) . . . . . | 25·12 |
| Substances insoluble in alcohol of 85% (pancreatic and intestinal ferments and insoluble salts) . . . . . | 9·55 |

In 100 parts of the substances soluble in alcohol there were contained: —

| | |
|---|---|
| Fat | 2·80 |
| Biliary acids in combination with soda | 65·96 |
| Taurine | 1·03 |
| Other organic matters | 14·80 |
| Inorganic constituents (chiefly chloride of sodium) | 15·41 |

B.

| | |
|---|---|
| Water | 969·58 |
| Soluble matters not volatile at 248° | 30·42 |
| Insoluble epithelial structures with earthy phosphates | 8·65 |
| Pancreatic and intestinal ferments soluble in water | 5·84 |
| Biliary constituents and salts soluble in alcohol | 15·93 |

It is obvious that in both these cases the intestinal juice was far from pure.

Its quantity.

(172.) The quantity of intestinal juice secreted in a given time, cannot be accurately determined; it seems, however, to reach its maximum in the small intestine five or six hours after a meal, and to be much and rapidly increased by the ingestion of fluids.* Schmidt estimates from a rough calculation, that an adult man weighing ten stones secretes in twenty-four hours about 300 grammes of intestinal juice.

Its functions.

(173.) The intestinal juice seems to unite in itself the leading powers of the pancreatic fluid and the gastric juice; that is to say, it resembles the former in converting starch into sugar, and the latter in dissolving flesh and the other protein-bodies.

Starch, in the form of paste, when introduced into loops of

* It is worthy of remark that the intestinal juice which flows abundantly after drink has been taken, exhibits the same concentration as before the ingestion of the fluid; hence it must be inferred that the drink is absorbed in the stomach, and perhaps in the upper part of the small intestine, and that the water which thus finds its way into the blood, increases the intestinal juice in common with the other secretions.

gut tied at both ends and re-introduced into the abdominal cavity, was usually found in Schmidt's experiments to be converted in the course of three hours into a thin fluid mass, which no longer yielded any reaction with iodine, but gave undoubted evidence of the presence of sugar. On mixing together starch-paste and intestinal juice out of the body at a temperature of about 100°, an abundance of sugar was found in the mixture in a quarter of an hour.

In a similar way pieces of flesh or coagulated albumen were introduced into tied loops, and in the course of from six to fourteen hours they were found to be for the most part or entirely dissolved. Schmidt also showed by experiments made externally to the organism, that the intestinal juice both when mixed with bile and pancreatic juice, as well as in its pure state, possesses the power of dissolving the protein-bodies. Kölliker and Müller,* and likewise Funke,† failed in observing any solvent action of the intestinal juice on the protein-bodies in the case of the rabbit, but the former observers afterwards fully confirmed Schmidt's results in experimenting on cats.

We have previously stated (see p. 165.) that a very large amount of albuminates passes undigested from the stomach, and that the quantity of gastric juice which is secreted is not sufficient to dissolve the protein-matters necessary for nutrition; and hence we should have concluded, *à priori*, that nature had provided some additional solvent for flesh, albumen, &c., and the same remark applies to the fluids which effect the metamorphosis of starch, for Schmidt has shown that the pancreatic juice is absorbed and disappears before it reaches the middle of the small intestine‡, and yet we find that starch is readily converted into sugar below that point.

* Verhandl. d. phys.-med. Gesellsch. in Würzburg. 1856, vol. vii. p. 509.

† See his edition of Wagner's "Lehrbuch d. Speciellen Physiologie," 1855, pp. 220 — 222.

‡ Schmidt found that the contents of the intestine are unable, beyond that

## SECTION VI. — THE CONTENTS OF THE INTESTINAL CANAL.

(174.) This section, which must be regarded as supplementary to the previous ones, includes the consideration of various substances for which it is not easy to find a better position, namely:— (1.) the semi-solid contents of the small intestine; (2.) the gases contained in the intestinal canal; (3.) vomited matters; (4.) the contents of the fœtal intestine and the meconium; and (5.) the excrements in health and disease.

### 1. — *The semi-solid Contents of the Small Intestine.*

Composition of intestinal contents.

(175.) On laying open the small intestine, we usually find an admixture of imperfectly digested and indigestible substances, associated with food which has already undergone change, and with the constituents of the digestive fluids in every stage of metamorphosis.

The reaction of the intestinal contents varies in different parts of the intestinal canal, and is to a certain degree dependent on the nature of the food. The contents of the stomach always redden litmus paper, whatever kind of food has been taken. The duodenal contents, notwithstanding the admixture of the bile and pancreatic juice, are likewise always acid, although in a far less intense degree than those of the stomach. In the jejunum, we usually meet with only a faint acid reaction, which altogether disappears in the ileum, while in the cæcum (and sometimes in the lower part of the ileum) an alkaline reaction is manifested. After a purely flesh-diet, the acid reaction disappears shortly below the duodenum, while after the ingestion of vegetable food it often extends through more than half the small intestine, and sometimes (especially after the use of sugar) to the cæcum. As a

point, to separate butyric acid from butter, which is a property of the pancreatic juice.

general rule, the contents of the large intestine are alkaline; it very often, however, happens that the interior of the mass is strongly acid, while the outer parts which are moistened with the intestinal juice are neutral or alkaline.

The acid reaction presented by the contents of the stomach is mainly due to the free acid of the gastric juice, and in the duodenum the free acid is chiefly dependent on the same sources, although the liberated and as yet undecomposed biliary acids may co-operate in producing this acid reaction. The lactic acid which is found in the lower part of the small intestine, and in the large intestine after the free use of starch or sugar, is unquestionably mainly due to the decomposition and fermentation of the food, and must not be regarded as a secretion from the intestinal walls; and the butyric acid that is occasionally found in these parts must be referred to a similar source. We have already (see pp. 32-33.) noticed the possibility of leucine slightly contributing to the development of volatile fatty acids in the intestine. The alkaline reaction of the contents of the large intestine is chiefly due to the preponderance of the alkaline intestinal juice; Lehmann believes, however, that it may be sometimes increased by a development of ammonia.

Soluble constituents.

In consequence of the rapid absorption that goes on along the intestinal surface, we meet with a comparatively small proportion of soluble matters in these contents. Amongst these soluble matters we often find *glycose*, which seems to owe its origin to the action of the pancreatic fluid and intestinal juice upon starch, and not to sugar having been present in the food; for after saccharine food has been taken we very rarely meet with this substance in the small intestine, and then only in its upper part, its absorption taking place with great rapidity.

Glycose.

A coagulable protein-body.

In the aqueous extract of the contents of the small intestine we always find small quantities of a *protein-body* coagulable by heat and usually precipitable by acetic acid. Since the

protein-bodies are converted during digestion (see p. 163) into soluble but *non-coagulable* substances (the peptones); since the coagulable matter of the pancreatic juice (the pancreatic diastase or ferment) is soon absorbed by the intestine (see the note to p. 185.); and since, further, this coagulable protein-body is equally found in the intestine after the use of vegetable food poor in protein-bodies, and even of non-nitrogenous food, it seems almost certain that the origin of this substance must be referred to an exudation of albuminous matter from the intestinal capillaries in accordance with the laws of endosmosis.

Dextrine and peptones.

In the filtered contents of the small intestine we only rarely find *dextrine* (Lehmann never succeeded in detecting it), and never more than small quantites of *peptones.*

Biliary constituents.

In the alcoholic extract of the intestinal contents we can almost always obtain evidence of the presence of *biliary constituents.* In the duodenum and for a little way beyond it we find the unchanged conjugated biliary acids; as we descend further we find less of these acids, but a comparatively larger amount of the products of their disintegration, namely, choloidic acid, taurine, and dyslysin; while in the large intestine we have usually little more than a trace of choloidic acid and taurine. These chemical observations are confirmatory of experiments instituted by Schmidt, which show that nearly half the bile which is poured into the duodenum is decomposed before it reaches the middle of the small intestine.

Bile-pigment.

The *bile-pigment* undergoes the same changes in the intestinal canal as are observed to occur in the decomposition of the bile. In the alcoholic extract of the contents of the small intestine we usually obtain the well-known changes of colour on the addition of nitric acid (see p. 96). The yellowish-brown colour of the excrements is apparently due to highly oxidised bile-pigment.

*Cholesterin* is always to be detected in the intestinal contents, and is doubtless derived from the bile. Cholesterin.

A little *fat* is usually found along the whole course of the intestinal canal, especially after an animal diet. Fat.

Amongst the *insoluble constituents* of the intestinal contents may be mentioned almost all remains of undigested or indigestible food, such as starch-granules, partially dissolved muscular fibre, fragments of bone, various constituents of the vegetable tissues, yeast-cells *, &c. Insoluble residue.

## 2. — *The Gases contained in the Intestinal Canal.*

(176.) The gases which are found in the intestinal canal owe their origin partly to air conveyed into the stomach from without, partly to the decomposition of the intestinal contents, and partly to an interchange of the preceding gases with those contained in the blood of the intestinal capillaries. The most trustworthy observations on the nature of these gases are those instituted by Magendie and Chevreul, who examined the gaseous contents of the stomach and small and large intestines of three criminals immediately after their execution, and those of Valentin on two horses which he killed by bleeding. Intestinal gases.

The following are the results obtained by Magendie and Chevreul: —

| | Stomach. | Small Intestine. | | | Large Intestine. | | |
|---|---|---|---|---|---|---|---|
| | | 1. | 2. | 3. | 1. | 2. | 3. |
| Carbonic acid . . | 14·00 | 24·39 | 40·00 | 25·00 | 43·50 | 70·0 | 22·50 |
| Oxygen . . . . | 11·00 | — | — | — | — | — | — |
| Nitrogen . . . | 71·45 | 20·08 | 8·85 | 66·60 | 51·03 | 18·4 | 67·50 |
| Hydrogen . . . | 3·55 | 55·53 | 51·15 | 8·40 | — | 11·6 | 7·50 |
| Carburetted hydrogen | — | — | — | — | 5·47 | | 12·50 |

* These are stated to be of common occurrence after the use of pastry.

The hydrogen and that part of the carbonic acid which is not derived from the blood are products of fermentation; and we may suppose them produced in the following manner:—

2 at. lactic acid ($C_{12}H_{10}O_{10}$) + 2 at. water ($H_2O_2$) = 1 at. hydrated butyric acid ($C_8H_8O_4$) + 4 at. carbonic acid ($C_4O_8$) + 4 at. hydrogen ($H_4$).

Flatus passed from the anus presents much the same composition as the gas found in the large intestine, but it usually has a more marked fæcal odour. In two analyses of such flatus Marchand found:—

| | | |
|---|---|---|
| Carbonic acid . . . | 44·5 | 36·5 |
| Nitrogen . . . . | 14·0 | 29·0 |
| Hydrogen . . . . | 25·8 | 13·5 |
| Carburetted hydrogen . | 15·5 | 22·0 |
| Sulphuretted hydrogen . | 1·0 | — |

Valentin's analyses are probably the most accurate, but in consequence of the different nature of the food it is uncertain how far the gases found in the intestinal canal of the horse correspond with those occurring in the human subject. The two horses are indicated by A and B.

| | Stomach. | | Upper part of small Intestine. | Middle part of small Intestine. | Lower part of small Intestine. | Cæcum. | | Middle portion of Rectum. |
|---|---|---|---|---|---|---|---|---|
| | A. | B. | A. | B. | B. | A. | B. | A. |
| Carbonic acid | 44·35 | 55·64 | 18·83 | 41·78 | 19·41 | 77·70 | 71·59 | 47·94 |
| Oxygen . . | 7·16 | 0·77 | 5·76 | — | 4·97 | — | — | — |
| Nitrogen . | 44·23 | 25·38 | 73·35 | 48·70 | 73·31 | 10·23 | 16·32 | 24·39 |
| Hydrogen . | 0·66 | 13·29 | — | 0·02 | 0·08 | 4·67 | 0·20 | 13·82 |
| Carburetted hydrogen | 0·90 | — | 0·45 | 4·98 | 0·77 | 4·09 | 6·96 | 11·82 |
| Sulphuretted hydrogen | 2·70 | 4·92 | 1·61 | 4 52 | 1·46 | 2·02 | 3·71 | 0·54 |
| Ammonia . | — | — | — | — | — | 1·29 | 1·22 | 1·49 |

The coincidence of an excess of carbonic acid in the stomach and the cæcum seems to be in connection with the digestive function which the latter organ discharges in the

herbivora. Valentin agrees with previous observers regarding the total absence of oxygen in the gases of the large intestines. The relatively large quantities of carburetted hydrogen and hydrogen in the rectum show, he thinks, that changes in the remains of the food continue to take place up to the last portions of the digestive canal.

In cases of morbid digestion, I have occasionally met with such an abundance of sulphuretted hydrogen in the eructations as to be very unpleasant to the patient. These cases are, I believe, generally associated with the presence of oxalate of lime in the urine, and both symptoms usually disappear under the use of the mineral acids.

### 3. — *Vomited Matters.*

Vomited matters.

(177.) It is unnecessary to notice that kind of vomit which consists of partly digested food mixed with the digestive fluid. The matters which in certain diseases are vomited in the fasting state, and which are actually secreted fluids, are, however, of sufficient pathological importance to merit a notice in this section.

In gastric disease.

In many forms of gastric disease, as for instance in the chronic gastric catarrh of drunkards, and sometimes in cancer and perforating ulcer of the stomach, there is an abundance of saliva secreted which accumulates in the stomach, and finally induces vomiting. In such cases the vomited matters present all the characters of saliva; they are usually alkaline, but sometimes neutral or even acid, contain sulphocyanides, and have the power of converting starch into sugar.

In cholera.

The rice-water matters vomited in cholera have been frequently analysed. They usually present a faint mawkish odour, and their reaction may be acid, neutral, or alkaline. On standing they deposit epithelial structures (usually cylindrical epithelium) and mucus, the supernatant fluid being clear and yellowish The fluid contains little organic matter,

but a relatively large amount of inorganic salts, chiefly chloride of sodium. In the early stage, the vomited matter is acid, and butyric and acetic acids have been detected in it. When the fluid is acid or neutral, and contains no remains of food, urea is constantly present. If, on the other hand, the disease is further advanced, and symptoms of uræmia are established, the vomited matter contains carbonate of ammonia, and consequently has an alkaline reaction. Albumen occurs only very sparingly when the fluid is acid, but more abundantly when there is an alkaline reaction.

In searching for biliary constituents or blood in vomited matters, it must not be forgotten that the free acid of the gastric juice may very much modify them. For instance, in certain forms of peritonitis and cerebral inflammation, we may have a grass-green colour developed from the action of the acid on the brown bile-pigment; and similarly the action of the acid on the blood-corpuscles may give rise to those varieties of brown or black vomit with which most physicians are familiar.

### 4.— *The Contents of the Fœtal Intestine and the Meconium.*

The Meconium.

(178.) According to Lehmann, the small intestine of the human fœtus, between the fifth and sixth month, always contains a bright yellow mass, which is either neutral or faintly acid. From 89 to 96% of the solid residue of this mass is composed of epithelial structures and mucus, while the remainder consists of oleic and margaric acids, a little fat, taurocholate and glycocholate of soda, a casein-like substance (probably albuminate of soda), and the chlorides of sodium and potassium. The presence of bile in the fœtal intestine is confirmed by an examination, made by Schlossberger, of the yellow mucus contained in the small intestine of a fœtal calf at the fortieth week, which yielded indications both of the biliary acids and of bile-pigment.

The contents of the large intestine of the fœtus in and after the seventh month are almost perfectly identical with the meconium discharged after birth; occurring in tolerably compact masses of a brownish green or almost black colour, without odour, and rapidly putrefying on exposure to the air. As a general rule, Lehmann has found the contents of the large intestine, as well as the meconium, acid; occasionally, however, they are neutral. The microscope reveals the presence of an abundance of cylinder epithelium of a beautiful green tint, of mucus-corpuscles, and of fat (with which there is a good deal of cholesterin). Neither the biliary acids nor bile-pigment can be detected in it, nor does it contain any substance precipitable by heat or acetic acid.*

### 5.— *The Excrements in Health and Disease.*

(179.) The solid excrements, or the fæces, consist of a mixture composed of undigested particles of food (such as vegetable cellular tissue, fragments of tendon, skin, half-digested muscular fibre), of epithelium and mucus (derived from the intestinal walls), and of traces of the decomposed biliary constituents. The Fæces.

After the use of fatty food, a considerable quantity of fat may be found in the excrements, in consequence of the comparatively small power which the intestine possesses of absorbing that substance, as has been shown by the experiments of Boussingault and others; and when starch or sugar has been taken freely, sugar (although only in small quantity, in consequence of the readiness with which it is absorbed) is often present. Moreover, the excrement always

* In an analysis of meconium made by Simon, both casein and albumen were found in very considerable quantity. Dr. Davy, however, like Lehmann, did not find any protein-body. The analyses of Simon and Davy may be seen in my Translation of "Simon's Animal Chemistry," Lond. 1846, vol. ii. pp. 367-369.

contains a certain amount of salts, whose composition will presently be noticed.

Their odour.

The peculiar odour of the fæces is chiefly dependent, according to Valentin, on the decomposed bile; while Liebig refers it to a decomposition of albuminous matters, founding his view on the fact that something like a fæcal odour may be produced by burning albumen with potash. In consequence of the small quantity of albumen in the contents of the large intestine, the former view is the more probable, and it is further supported by the circumstance that the peculiar fæcal odour disappears, and is replaced by a strong putrid smell, when, as in cases of jaundice, the bile does not flow into the intestine.

Their colour.

The colour of the normal fæces varies with the food; on a mixed diet they are of a yellowish-brown tint, on a flesh diet much darker, and on a milk-diet quite yellow. On exposure to the air the colour becomes darker; and, on the addition of very dilute nitric acid a red tint is always developed.

The consistence seems chiefly to depend upon the constitutional relations of the individual; but it is considerably influenced by bodily exercise. As a general rule the longer the excrements are retained in the intestine the greater is their consistence.

The reaction is most commonly alkaline, but no very definite rule can be laid down on this point. According to Marcet, the reaction is constantly alkaline; according to Lehmann and Wehsarg, generally acid, but very often alkaline or neutral.

Their daily quantity.

The quantity of the daily fæces is very variable. The mean of seventeen observations made by Wehsarg * was 131 grammes (or about 4·6 ounces), the largest and smallest quantities being 306 and 67·2 grammes respectively. There is no definite relation between the amount of fæces and the

* Mikroskopische und chemische Untersuchungen der Fæces gesunder erwachsener Menschen. Giessen. 1853.

bodily weight; the quantity of fæces seems rather to be connected with the digestive power of the individual.

The fæces, when in a formed or half-formed state, contain on an average 73·3% of water and other matters volatile at 248°, and 26·7% of solid constituents; in seventeen observations the latter varied from 17·4 to 31·7%.

The absolute quantity of solid matter discharged in the twenty-four hours averages thirty grammes (or rather less than one ounce); the extremes being 57·2 and 16·3 grammes.

The amount of *undigested matters* varies very much in different cases, the mean quantity in ten observations was 3·4 grammes (about fifty-two grains), or 8·3%; the extremes being 8·2 grammes and 0·81 of a gramme.

The ether-extract of the fæces varies extremely, according to Wehsarg, with the nature of the food. After a very fatty diet it rose to 31·2 grammes (about an ounce) or 58·2% of the dried residue; the mean was 11·5%, and the minimum 8·5%. It consisted for the most part of a waxy fat.

The alcohol-extract was found to amount (as the mean of three observations) to 15·6%, and it may rise to double this quantity in diarrhœa. Wehsarg could only once detect the presence of bile in it with certainty, although he often got doubtful indications; and on the addition of nitric acid to fresh fæces, he only twice obtained undoubted evidence of bile-pigment.

The water-extract is a brownish-black mass which undergoes decomposition on drying, and averages about 20% of the dry fæces.

Their mineral constituents.

Liebig, many years ago, made the observation that the solid excrements contain only a small amount of soluble salts, these being mainly carried off by the urine. The mineral constituents have been examined by Berzelius, Enderlin, Lehmann, Fleitmann, and Porter, and, as a general result, it may be stated that the mineral constituents yielded by the incineration of dried human fæces amount on an average to

6·7%, of which only 1·54 (or 23% of the ash) are soluble salts. Berzelius first directed attention to the fact that more lime than magnesia must be absorbed in the intestine, since we find in the solid excrements less lime and relatively more magnesia than in the food that has been taken; the ratio of the magnesia to the lime in the excrements being as 1 : 2 or 1 : 2·5. In 100 parts of ash, Fleitmann found 21·36 of lime with 10·67 of magnesia, and Porter 26·46 of lime with 10·54 of magnesia. The principal acid which occurs in the fæces in combination with the earths and alkalies, is tribasic phosphoric acid, which, according to Fleitmann, forms nearly 31, and according to Porter, more than 36% of the fæcal ash. Crystals of phosphate of ammonia and magnesia may often be detected by the microscope in perfectly normal evacuations of a neutral or alkaline reaction, although they are far more abundant in those diseases in which the contents of the bowels are especially prone to decomposition, as in typhus, cholera, and certain forms of dysentery.

A certain amount of silica, taken either as sand with various articles of food (as, for instance, brown sugar) or in the siliceous structure of various plants, is always found in the excrements. Berzelius found that the fæcal ash contained more than 12, and Enderlin nearly 10% of this constituent.

Undecomposed bile only occurs in the excrements when the intestinal contents pass more rapidly than usual through the bowels; as, for instance, after the use of saline and acrid purgatives and in certain forms of diarrhœa. Pettenkofer's test will then reveal its presence: taurine may, however, be regarded as a common if not a constant ingredient of the fæces.*

* In the preceding remarks I have refrained from noticing Dr. Marcet's recent investigations in consequence of their comparative incompleteness. His principal conclusions are that human evacuations in the healthy condition contain: — 1. A new organic immediate principle, which he terms *excretine*, having a crystalline structure, an alkaline reaction, and represented by the formula $C_{78}H_{78}SO_2$. 2. A substance possessing the character of margaric acid, which is chiefly found after the use of vegetable food, and occurs mostly

(180.) The bright yellow semifluid excrements of infants at the breast contain, as was shown by Simon *, a large quantity of fat, a considerable amount of coagulated bile, undigested casein, and a sufficient quantity both of the biliary acids and bile-pigment to give certain evidence of the presence of these bodies by Pettenkofer's test and by nitric acid respectively. Epithelial structures are moreover present. Yellow excrement of infants.

(181.) The excrements sometimes present a green colour, which, until comparatively recently, was regarded as a sign of the presence of an excess of bile. This is, however, seldom the cause of a green colouration of the fæces, and only occurs when there is at the same time an excess of bile and a preponderance of free acid in the intestine; as, for instance, in *icterus neonatorum*. In these cases the ordinary brown bile-pigment seems to be converted into the modification termed bilifulvin. As we shall presently show, the presence of blood may sometimes give rise to a green colour. Green excrements.

Lehmann has confirmed the observations of Höfle and others, regarding the occurrence of sulphide (sulphuret) of mercury in the green or greenish-black stools that are voided after the use of calomel. The colour in this case seems due partly to the presence of almost unchanged bile, and partly to that of the mercurial compound.

The excrements often assume a black or dark green colour after the prolonged use of ferruginous preparations or chalybeate waters (especially such as contain sulphate of soda with carbonate of protoxide of iron). Lehmann has definitely shown, from analyses of the green and black excrements of persons taking the Marienbad waters, that the colour is here due to the presence of protosulphide of iron.

free, but partly in combination with lime and magnesia. 3. A colouring matter analogous to that of the blood. 4. An olive-coloured fatty acid, for which he proposes the term *excretoleic acid*. 5. Volatile fatty acids, free, however, from butyric acid.

* Animal Chemistry, vol. ii. p. 369.

The excrements are usually green after the medicinal use of indigo, and are often black after charcoal has been taken.

Fat.

As only a definite quantity of fat can be absorbed by the intestines in a given time, food very rich in fat or the ingestion of cod-liver or other oils may give rise to the presence of a large quantity of fat in the excrements. In some diseases, especially such as specially interfere with the general nutritive processes, such as pulmonary phthisis, Bright's disease, diabetes mellitus*, and more particularly diseased conditions of the pancreas, an augmentation of the fat in the fæces is often observed.

Sugar has been occasionally found, but it is not always present, in the excrements of diabetic patients.

Blood.

The occurrence of blood in the fæces is by no means rare. Omitting all notice of those cases in which its presence is too obvious to be overlooked, we may remark that when the hæmorrhage is very slight, and proceeds from the stomach or small intestine, it may impress upon the fæces a peculiar colour and appearance, whose cause may easily escape recognition. In such cases we often have black or chocolate-coloured tar-like stools, in which imperfect blood-corpuscles can be discovered by the microscope, and in which hæmatin can be chemically detected. In some of the intestinal diseases of young children, and occasionally in some forms of continued fever, semi-fluid green excrements are discharged which owe their colour to a slight admixture of blood which may be readily detected by the microscope.

Albumen in a coagulable state sometimes occurs in normal excrements; it is, however, found in large quantity in the evacuations in dysentery and in typhus (and not unfrequently

* Several analyses, showing the large quantity of fat occurring in the fæces of diabetic patients, may be found in Simon's "Animal Chemistry," vol. ii. pp. 377-79.

in the fluid or semi-fluid stools which sometimes occur in Bright's disease), and in lesser quantity in cholera.*

Epithelial structures occur in the stools in all cases of diarrhœa. They are extremely abundant in the evacuations in cholera. (See *Pl. V. fig.* 2.)

Cytoïd corpuscles are abundant in the evacuations in intestinal catarrh and in dysentery; and are occasionally observed in typhus and cholera. The glassy mucus which sometimes occurs in roundish masses in catarrhal affections of the large intestines is apparently secreted by the follicles of the colon.

The intestinal evacuations have been especially studied in typhus and cholera.

Fæces in disease.

(182.) In typhus the stools are usually fluid, of a yellowish brown colour, an abominable smell, and an alkaline reaction. On standing for some time they separate into a yellowish sediment, consisting of flakes of undigested food, white granules of about the size of a pin's head and probably resulting from intestinal ulcers, epithelium, and often mucus, and numerous crystals of phosphate of ammonia and magnesia; and an opaque supernatant fluid of a yellowish or pale brown tint, generally containing albumen and a large quantity of chloride of sodium.

In cholera the main peculiarities of the stools are, in addition to the abundance of epithelium already referred to, an extraordinary quantity of water, a little albumen, very little biliary matter, and a large amount of salts, among which the chloride of sodium preponderates to such an extent as often to exceed in amount all the organic matters. These evacuations contain only from 1·2 to 2·4% of solid constituents. The addition of nitric acid gives rise to a rose-red tint in

* In testing the evacuations (especially in cholera) for albumen, we must neutralise the fluid matters with acetic acid before boiling, as they usually have an alkaline reaction.

these stools, which is often also observed in the evacuations in typhus.

Intestinal concretions.

(183.) Intestinal concretions are rare in man and in carnivorous animals, but are not uncommon in herbivorous animals. They usually consist of phosphate of ammonia and magnesia with some phosphate and carbonate of lime, which have deposited themselves round a fragment of undigested food. They are of no special physiological interest.*

* Further information on intestinal concretions may be found in Vogel's "Pathological Anatomy," London, 1847, pp. 375-381, and in Meckel von Hemsbach, "Ueber die Concremente im thierischen Organismus," Berlin, 1856, pp. 182-188.

# CHAPTER XI.

## THE BLOOD AND ITS ALLIES.

### SECTION I. — THE BLOOD.

(184.) The blood, as it exists in the circulating system of the higher animals, is a somewhat thick, viscid fluid, heavier than water, usually of a bright cherry-red colour (the arterial blood being of a lighter red than the venous), and only very slightly transparent. It undergoes a change immediately after its removal from the body, becoming more thick and gelatinous, and finally separating into two distinct parts, a solid dense dark-red mass, termed the clot or crassamentum, and a clear, pale yellow fluid, the serum. The blood; its physical characters.

The blood while still warm, has a peculiar odour, which is rather stronger in man than in woman, and is much more marked in some other animals than in man *; and it is apparently due to the presence of one of the volatile fatty acids in combination with an alkali.

The specific gravity of human blood varies from 1·045 to 1·075, the average being 1·055; in women it is somewhat lower than in men, in children less than in adults, and in pregnancy it is somewhat diminished. Specific gravity.

* Barruel's test is based on this circumstance. He maintained, in a memoir published in 1829, that by the addition of a little sulphuric acid to blood he could distinguish by the odour that was developed whether the blood was taken from a man, woman, ox, horse, sheep, goat, dog, pig, rat, &c. The experiments of Schmidt show, however, that Barruel's test is not so general in its application, and that it only gives characteristic results with the blood of the goat, sheep, and cat (Die Diagnostik verdächtiger Flecke in Criminalfällen, 1848).

The temperature of the blood very slightly exceeds that of the tissues of the body; in man the thermometer, when inserted into a vein, seldom rises above 102° (Nasse). The blood leaving the liver by the hepatic veins has a higher temperature than the blood of any other part of the body.*

Coagulation.

(185.) The coagulation of the blood may be divided into three stages. In from two to five minutes after its discharge from the body, the blood becomes viscid, tough, and almost gelatinous on its surface. In from seven to fourteen minutes the consistence has so far increased that the whole mass assumes the form of the vessel in which it has been placed. After the expiration of this time, we observe on the surface a thin layer of colourless or pale yellow fluid, which is found also to surround the sides and bottom of the clot; this is the serum, and its quantity increases as the fibrin — on which the coagulation of the blood depends — continues to contract, until at length, after from twelve to forty hours, the clot attains its minimum volume, and no more serum is expressed. The clot usually retains in a lessened size the shape of the vessel in which the blood contracted. The lower part of the clot is of a darker and the upper surface of a lighter red than the blood itself. The blood of men coagulates more slowly than that of women, and the clot is denser. Arterial blood coagulates more rapidly than venous blood. Free access of atmospheric air hastens coagulation. On shaking or stirring (or as we generally term it, whipping) freshly drawn blood we prevent the formation of one consistent clot, and the coagulating substance, the fibrin, separates in yellow or reddish flakes, while the fluid remains as red and opaque as coagulated blood.

Morphotic constituents.

(186.) We are indebted to Malpighi (1666) for the discovery that the blood is not a mere solution of various substances, that is to say, a homogeneous fluid, but an emulsion,

* Bernard, Leçons de Physiologie Expérimentale appliquée à la Medecine, 1855, vol. i. p. 201.

in which solid particles are suspended. Of these particles, by very far the greatest number are the minute bodies known as the red corpuscles, intermixed with which are the colourless or lymph-corpuscles, a few fat-globules, and occasionally an epithelial cell.

Red corpuscles.

The red corpuscles (to which the terms blood-corpuscles and blood-discs are often applied) differ in size and form in different kinds of animals. In all mammals, excepting the camel, dromedary, and llama, they form thick, circular, slightly biconcave discs, which are composed of a colourless investing membrane, containing a thick fluid, which is red in reflected, and yellow in transmitted light. (See *Pl. V. fig.* 3.) One or more amorphous granules may sometimes be observed in these blood-corpuscles, but it is now almost universally admitted that they do not contain a true nucleus.

In the camel, dromedary, and llama, the blood-corpuscles are elliptic and biconvex, resembling in these respects the blood-corpuscles of birds, reptiles, and fishes.

Human blood-corpuscles have an average diameter of about 1-3200th of an inch. The blood-corpuscles of the embryo are a little larger than those of the same animal after the establishment of respiration. In most mammals, excepting the elephant, they are rather smaller than in man. By far the largest corpuscles occur in the amphibia.*

Colourless corpuscles.

Colourless or lymph-corpuscles are always present in the blood, but occur in far less numbers than the red corpuscles, the ratio in which they stand in normal blood being about 1 : 400. They are nearly spherical, larger than the red corpuscles and granular on their surface; they contain one, or sometimes two or more, rounded oval or reniform nuclei.

* Extensive tables of the measurement of the blood-corpuscles of different animals are given in Gulliver's edition of Hewson's works (printed for the Sydenham Society, 1846), pp. 237 244, in C. Schmidt's "Diagnostik verdächtiger Flecke in Criminalfallen," 1848 (at the end), and Milne Edwards's "Leçons sur la Physiologie et l'Anatomie Comparée de l'Homme et des Animaux," 1857, vol. i. pp. 83-90.

From their being rich in fat and deficient in ferruginous hæmatin, they are of lighter specific gravity than the red corpuscles; hence we find them suspended in considerable numbers in the serum or accumulated on the surface of the clot.*

The fat globules and epithelial cells require no special description.

Liquor sanguinis.

(187.) The fluid in which the above described morphotic elements are suspended has received the various names of liquor sanguinis, plasma, and intercellular fluid; in the circulating blood it contains in solution not only all the solid matters of the serum, but likewise the fibrin on which the coagulation of the blood depends.

Clot.

The clot or coagulum consists of the fibrin in a coagulated state, of the blood-corpuscles which are enclosed in its meshes in contracting, and of a certain amount of serum which escapes the pressure of the contracting coagulated fibrin, and moistens the interior.

Serum.

The serum which gradually exudes during the contraction of the clot has precisely the same composition whether we examine the first or the last drops of the expressed fluid; its average specific gravity is 1·028.

The elements or constituents of the blood arrange themselves differently in the living and in the dead fluid.

Living blood = corpuscles + liquor sanguinis (= dissolved fibrin + serum).

Dead blood = clot (= coagulated fibrin + corpuscles) + serum.

* Dr. Hirt, of Zittau, has recently published an elaborate memoir on this subject. He found, in experiments made upon himself, that before breakfast the white were to the red corpuscles as 1 : 1800; an hour after breakfast (the breakfast hour being eight o'clock) as 1 : 700, and between eleven and one o'clock as 1 : 1500. At one o'clock he dined, soon after which the white corpuscles became more abundant than even after breakfast, namely, as 1 : 400; while two hours afterwards they fell to 1 : 1475. Shortly after supper (the supper-hour being eight o'clock) they again rose to 1 : 550, while by eleven o'clock they again sunk to 1 : 1200. We thus see the close connection between the digestive process and the number of the white corpuscles (Müller's Arch. 1856, p. 174.).

(188.) It is self-evident from the preceding observations that the corpuscles and their viscid fluid contents must be very different in their composition from the liquor sanguinis or the serum.

Chemical composition of the corpuscles, liquor sanguinis, and blood.

The following table (drawn up by Lehmann, and based partly on his own and partly on Schmidt's analyses) shows at a glance the differences between the composition of the blood-corpuscles and that of the fluid in which they are contained: —

| 1000 parts of blood-corpuscles contain: — | | 1000 parts of liquor sanguinis contain: — | |
|---|---|---|---|
| Water | 688·00 | | 902·90 |
| Solid constituents | 312·00 | | 97·10 |
| Specific gravity | 1·0885 | | 1·028 |
| Hæmatin | 16.75 | Fibrin | 4·05 |
| Hæmatocrystallin | 241·07 | Albumen | 78·84 |
| Cell-membranes | 41·15 | | |
| Fat | 2·31 | | 1·72 |
| Extractive matter | 2·60 | | 3·94 |
| Mineral substances (excluding iron) | 8·12 | | 8·55 |
| Chlorine | 1·686 | | 3·644 |
| Sulphuric acid | 0·066 | | 0·115 |
| Phosphoric acid | 1·134 | | 0·191 |
| Potassium | 3·328 | | 0·323 |
| Sodium | 1·052 | | 3·341 |
| Oxygen | 0·667 | | 0·403 |
| Phosphate of lime | 0·114 | | 0·311 |
| Phosphate of magnesia | 0·073 | | 0·222 |

The two following tables exhibit the composition of male and female human blood. The analyses were made by Schmidt and were employed by Lehmann in the con-

struction of the preceding tables. The only modification that I have introduced is to separate his hæmatoglobulin (or blood-casein, as Schmidt terms it) into hæmatocrystallin and cell-membranes in the proportions in which the two latter substances normally stand to one another.

*Man aged* 25 *Years.* 1000 *parts of Blood* (*Sp. Gr.* 1·060) *contained:* —

| 513·02 of Blood-cells * | | + | 486·98 of Plasma. | |
|---|---|---|---|---|
| Water . . . . | 349·69 | | . . . . | 439·02 |
| Solid residue . . | 163·33 | | . . . . | 47·96 |
| Hæmatin . . | 7·70 | | | |
| (including iron 0·512) | | | Fibrin . . . | 3·93 |
| Hæmatocrystallin | 127·54 | | | |
| Cell-membrane, fat, and extractive matters . . | 24·35 | | Albumen, fat, and extractive matters . . | 39·89 |
| Inorganic constituents (exclusive of iron) . . | 3·74 | | . . . . . | 4·14 |
| Consisting of: — | | | Consisting of: — | |
| Chloride of potassium | 1·887 | | . . . . . | 0·175 |
| Chloride of sodium | — | | . . . . . | 0·701 |
| Sulphate of potash | 0·068 | | . . . . . | 0·137 |
| Phosphate of potash | 1·202 | | | — |
| Phosphate of soda | 0·325 | | . . . . . | 0·132 |
| Soda . . . | 0·175 | | . . . . . | 0·746 |
| Phosphate of lime | 0·048 | | . . . . . | 0·145 |
| Phosphate of magnesia . . . | 0·031 | | . . . . . | 0·106 |

* As I have purposely excluded all complicated analytical details from this volume, I must refer those who wish to ascertain how to determine the ratio of the blood-cells to the plasma to Schmidt's investigations on the composition of the blood in his "Charakteristik der Epidem. Cholera," 1850, pp. 16-19, or to Lehmann's "Physiological Chemistry," vol. ii. pp. 219-221.

*Woman* aged* 30 *Years.* 1000 *parts of Blood* (*Sp. Gr.* 1·050) *contained:* —

| 396·24 of Blood-cells | | + | 603·76 of Plasma. | |
|---|---|---|---|---|
| Water . . . . | 272·56 | | . . . . . | 551·99 |
| Solid residue . . | 123·68 | | . . . . . | 51·77 |
| Hæmatin . . . | 6·99 | | | |
| (including iron 0·489) | | | Fibrin . . . | 1·91 |
| Hæmatocrystallin | 95·01 | | | |
| Cell-membrane, fat, and extractive matters . . | 18·13 | | Albumen, fat, and extractive matters . . | 44·79 |
| Inorganic constituents (exclusive of iron) . . | 3·55 | | . . . . . | 5·07 |
| Consisting of: — | | | Consisting of: — | |
| Chloride of potassium | 1·353 | | . . . . . | 0·270 |
| Chloride of sodium | — | | . . . . . | 3·417 |
| Sulphate of potash | 0·062 | | . . . . . | 0·131 |
| Phosphate of potash | 0·835 | | | — |
| Phosphate of soda | — | | . . . . . | 0·267 |
| Potash . . . . | 0·340 | | | — |
| Soda . . . . | 0·874 | | . . . . . | 0·648 |
| Earthy phosphates | 0·086 | | . . . . . | 0·332 |

* Becquerel and Rodier have given the following general formula as representing the average composition of healthy human blood, as deduced from twenty-two cases: —

| | |
|---|---|
| Water . . . . . | 781·60 |
| Solid constituents . . . . | 218·40 |
| Blood-corpuscles . . . . | 135·00 |
| Albumen . . . . . | 70·00 |
| Fibrin . . . . . | 2·50 |
| Fatty matters . . . . . | 1·55 |
| Soluble salts . . . . . | 6·00 |
| Earthy phosphates . . . . | 0·35 |
| Iron . . . . . | 0·55 |
| Indefinite extractive matters . . | 2·45 |

From the preceding tables we at once perceive that not only are certain constituents peculiar to the blood-cells and to the plasma respectively (namely, hæmatin with its iron, hæmatocrystallin, and cell-membranes to the former, and fibrin and albumen to the latter), but that some of the constituents common to both preponderate in a remarkable degree in one or the other (namely, potassium and phosphoric acid in the former and sodium and chlorine in the latter).

Arrangement of the subject.

(189.) In accordance with the arrangement adopted in the preceding tables, we shall first consider the physical and chemical properties of the blood-corpuscles, and then those of the intercellular fluid or plasma, after which the differences presented by the blood under various physiological conditions and in various parts of the system; the modifications impressed upon this fluid by disease; and the blood of the lower animals will be duly noticed; while we shall conclude with a few remarks on one or two chemico-physiological points, as, for instance, the quantity of blood contained in the body, the functions of the blood-cells, &c.

The blood-cells; their physical characters.

(190.) The physical properties of the blood-corpuscles exert a considerable influence on some of the changes which certain physiological and pathological conditions impress upon the blood. The simplest diffusion-experiment shows that these blood-corpuscles are vesicles in which the contents differ physically and chemically from the cell-wall: in the intercellular fluid they maintain the form of biconcave discs; on the addition of water they become distended even to bursting; while solutions of neutral salts, sugar, or gum cause them to collapse. Hence in the circulating blood there are continuous endosmotic currents between the intercellular fluid and the viscid red fluid which occupies the interior of the blood-cells; and, as the former is more or less dense, so do the vesicles tend to collapse or expand. Hence the specific gravity of the blood-corpuscles is by no means constant, increasing when more water is withdrawn from them than

from the intercellular fluid, and diminishing when the latter becomes more than usually watery; moreover, they become specifically heavier after the abstraction of a portion of their salts and hæmatocrystallin, as occurs in the circulating blood after repeated bleedings; for the hæmatin (which is dense, from its iron) is then retained in the corpuscles in excess, and increases their weight (Lehmann*); and they become specifically lighter when they contain an excess of fat in the form of fine molecules, or when the blood is abnormally aqueous.

In men the density may normally vary from 1·0885 to 1·0889, and in women from 1·0880 to 1·0886. The highest density that has been observed is in cholera, where it has reached 1·1027, and the lowest in dropsy, where it has fallen to 1·0819; hence its ascending is much greater than its descending range.

The tendency to sink which the blood-corpuscles possess is doubtless mainly due to their specific gravity, but it seems to be also to a certain degree dependent on another physical property which they exhibit, that, namely, of arranging themselves like rolls of coins with their flat surfaces in contact (see *Plate V. fig.* 4). This nummular arrangement (as it has been termed) never occurs in quite fresh blood; it is usually most distinctly seen, under the microscope, after partial evaporation of the water of the blood. The tendency of the red corpuscles to arrange themselves in this manner has been referred, especially by Henle, to an augmented viscidity of the intercellular fluid induced by an excess of fibrin or albumen; and by Nasse to a peculiar viscidity in the cell-walls themselves: of these two views the latter is the more probable.

Variations in the sinking tendency.

In connection with the sinking tendency of the corpuscles Nasse finds that it differs very considerably in different

* Handbuch der Physiol. Chem. 1854, p. 103.

animals; they sink most rapidly in the horse, most slowly in the pig. The serum of horses' blood is certainly very viscid, but this viscidity cannot be the cause of the slow sinking, because the corpuscles of horses' blood sink just as rapidly in the serum of the blood of other animals, and because further the blood-corpuscles of other animals do not sink with greater rapidity in the serum of horses' blood. The fact that the corpuscles of horses' blood contain less fat than those of most other animals may have something to do with the rapid sinking.

The corpuscles sink more rapidly in inflammatory than in healthy blood, the former being richer in carbonic acid and rather poorer in albumen than the latter; as, moreover, they sink with equal rapidity in defibrinated inflammatory blood, the excess of fibrin which exists in this blood can have nothing to do with the sinking tendency.

Colour of the blood

(191.) The colour of the blood is dependent on several conjoined causes, amongst which may be especially mentioned, (1) the form of the corpuscles, (2) the thickness of their walls, (3) the admixture of strongly refracting or reflecting molecules, and (4) certain chemical relations.

1. Contracted biconcave corpuscles must act the part of minute concave mirrors, and by their reflection must communicate a light colour to the mass of the blood; while corpuscles distended by endosmosis into a convex shape must in a corresponding manner scatter and disperse the light and thus render the colour darker. In accordance with this view we find that all substances which, by abstracting water from the corpuscles, render them more biconcave, as, for instance, solutions of neutral salts*, of sugar, &c., and which exert no disintegrating action on the blood, communicate to

* The following are some of the salts producing these effects:—the sulphates and nitrates of potash and soda, chlorate of potash, phosphate, carbonate and bicarbonate of soda, ferrocyanide, iodide, and sulphocyanide of potassium, biborate of soda, hydrochlorate of ammonia, &c.

it a lighter tint; while substances which distend the corpuscles, such as water, ether, and diluted organic acids, communicate a deep purple tint to the blood. We must not, however, conclude that the concavity of the corpuscles is the main cause of the light colour of the blood, for the blood of the amphibia which contains biconvex corpuscles (which cannot be rendered biconcave) also becomes of a light tint on the addition of a solution of the neutral salts, or of sugar.

2. Scherer, who has very carefully studied the influence of the form of the corpuscles on the colour of the blood, has shown that the change of form must necessarily be accompanied by an alteration in the thickness of the cell-walls, which must likewise modify the tint of the blood. If the corpuscles are collapsed the cell-walls will be relatively thick, and will conceal the pigment in the interior; while if they are distended their cell-walls will be relatively thin, and will allow the dark red colouring matter to shine through them, just as the colour of any dark red fluid is modified according as it is seen through a thick or a thin ground-glass vessel. On this account all substances which cause the cell-wall to burst, or which dissolve it, as, for instance, acetic acid, the alkalies, &c., communicate a dark red colour to the blood in consequence of the dissolved hæmatin mixing with the intercellular fluid.

From observations of Harless on the large biconvex blood-corpuscles of the frog, it appears that oxygen causes a contraction and carbonic acid an expansion of these bodies; hence a plausible explanation has been given of the difference in colour between arterial and venous blood.

3. There are often physical relations not directly acting on the blood-corpuscles which may modify the colour of the whole blood. Scherer showed that the addition of milk or of powdered gypsum made the blood of a lighter red tint, and a similar effect is produced when the blood contains a great excess of colourless corpuscles (as often occurs in anæmia and

always in leucæmia) or when it abounds in fat-globules (as in the case of confirmed drunkards).

4. The observations of Harless, to which reference has already been made, indicate that although the primary action of oxygen and carbonic acid is mechanical, these gases likewise exert a chemical influence on the blood-corpuscles: thus he found, for instance, that when we allow these gases to act alternately on the red corpuscles they become gradually destroyed, the destruction being usually completed after the ninth or tenth time.

The observations of Lehmann and others show that in a similar manner that action of saline substances, &c., although primarily mechanical, is also chemical. But whether these substances, and more especially the gases, in addition to acting on the cell-walls, extend their influence to the contents and especially to the pigment, is a question which is not very easily answered. It is true that as yet we are unacquainted with any special compounds of blood-pigment with oxygen or with carbonic acid, but the following facts lead to the belief that such compounds exist.

Dichromatism of the venous blood.

(192.) "Arterial blood, or blood which has been impregnated with oxygen, appears, in thin layers, of a beautiful scarlet colour, from a bright yellowish red to a dun colour; while venous blood or blood impregnated with carbonic acid, hydrogen, or nitrogen, appears, when seen in thin layers, of a purple colour; while in extremely thin layers it appears green. The latter, therefore, exhibits *dichromatism*, which is not the case with the former. Since artificially prepared hæmatin is monochromatic after the addition of acids, and dichromatic after being treated with alkalies, the difference in colour, effected by the action of oxygen or carbonic acid, can scarcely be referred to purely mechanical conditions.

"Blood which has been so diluted with water that no red corpuscles can be any longer recognised by the microscope, always becomes somewhat lighter coloured by oxygen and

darker by carbonic acid. The dark red solution of pure hæmatocrystallin also becomes of a somewhat lighter tint by oxygen, but of a still darker red by carbonic acid. That these gases also combine chemically with other protein-bodies is apparent from the fact that a solution of the globulin of the crystalline lens is entirely precipitated by carbonic acid, and that the precipitate is redissolved by the action of oxygen. On the other hand, the metameric hæmatocrystallin when treated with acetic acid and alkaline salts exhibits the opposite reaction, being precipitated from its solution by oxygen and redissolved by carbonic acid.

"After the preceding remarks it is almost unnecessary to observe that dilute acids exert a chemical action on the cell-walls of the blood-corpuscles; but those salts also, which at first produce contraction of the blood-cells and thus cause the colour of the blood to become lighter, exert a gradual destructive action on the cell-walls, so that the blood-corpuscles not only become altered in their form, but after a longer or shorter time are entirely destroyed, and, as a natural consequence, the colour of the blood, which was at first light red, passes into a deep dark red. The alkaline sulphates and nitrates maintain the vermilion colour of the blood for a considerable time; but with alkaline carbonates and hydrochlorate of ammonia the dark red tint very rapidly supervenes." *

(193.) The last physical property of the blood-corpuscles requiring notice is, that on filtering the blood they, for the most part, pass through the filtering paper. They, however, lose this property if concentrated solutions of the sulphate of soda or potash be previously added to the blood, and in this way a quantitative analysis of the blood-corpuscles has been

* Lehmann, Handbuch d. Physiol. Chém. Leipz. 1854, p. 107. The discovery of the dichroism (or dichromatism) of venous blood (referred to in the above quotation) is due to Brücke (Sitzungsbericht d. Wiener Akademie, vol. xi. p. 1070).

attempted. Dumas recommends that in order to check the clogging of the filter (which soon ensues) a stream of oxygen should be continuously passed into the fluid lying in the filter, while at the same time the solution of the alkaline sulphate should constantly drop into it.

(194.) The chemical characters of the blood-corpuscles now claim our attention. We shall consider first the cell-membrane, and secondly the fluid contents of the corpuscles.

The cell-membrane of the red corpuscles.

The cell-membrane, which formerly was erroneously supposed to consist of fibrin, and more recently of Mulder's binoxide of protein, forms in a state of purity and while still moist, a grayish-white viscid mass, which swells and assumes a gelatinous appearance in acetic acid and dilute alkalies, does not dissolve in nitre-water even after prolonged digestion at 100° F., contains no sulphur, and behaves towards nitric and hydrochloric acids like a protein-body.*

Two circumstances render it probable that the substance of the cell-walls has not always a precisely identical composition.† In the first place the addition of much water, or of ether, or acetic acid, affects the corpuscles of every kind of blood very unequally; some of them, probably the oldest, disappearing on the addition of very little water, while others (which we consider to be the youngest cells) do not appear changed even after great dilution. Secondly, no addition of water can cause the entire disappearance of the cells of the blood of the hepatic veins; the cells sinking to the bottom and forming a considerable deposit in the diluted blood.

* Lehmann's experiments on this substance are recorded in his Physiolog. Chemistry (Cav. Ed.) vol. ii. p. 184. In his most recent work (Handbuch d. Physiol. Chem., 1854, p. 108) he recommends the following as the best mode of obtaining the substance of the cell-membranes. Hæmatocrystallin prepared from the fluid of the blood-cells and containing many cell-membranes enclosed in its crystals, must be first rinsed with very diluted spirit till nitrate of silver ceases to yield any reaction, and then be treated with distilled water, which dissolves the pure hæmatocrystallin but does not act upon the membrane-substance, which, after extraction with alcohol and ether for the removal of any traces of fat, may be regarded as pure.

† Handbuch d. Physiol. Chem. 1854, p. 109.

(195.) The ratio in which the moist blood-cells stand to the plasma or intercellular fluid seems to be very variable even in normal blood. According to Lehmann the moist cells in the case of adults amount on an average to 51·2% of the blood, the limits being 47·2 and 54·2. In the only analysis of a healthy woman's blood given by Schmidt *, the cells, however, fall far below Lehmann's limit, amounting only to 39·6%. The blood of women, especially during pregnancy, is somewhat poorer in cells than that of men. Repeated venesections and other losses of the animal fluids are said to diminish their number, but Schmidt's investigations of the blood of cholera patients do not bear out this assertion. The blood of the pig is richer in corpuscles than that of any other mammal. In the amphibians the number of corpuscles is relatively smaller than in any other vertebrated animals.

Ratio of the blood-cells to the plasma.

Several observers have recently attempted to determine the number of red corpuscles in a given volume of healthy human blood. Vierordt found that on an average 1 cubic millimetre (which = 0·1055 or about 1-9th of a cubic line) of normal blood, obtained by pricking the finger, contained 5,055,000 corpuscles; Welcker† fixes the number at 4,600,000; and Cramer ‡ at 4,726,400.

(196.) Hæmatin and globulin have been, until very recently, regarded as the main constituents of the contents of the blood-corpuscles, the globulin being supposed to be identical with the substance of that name obtained from the crystalline lens of the eye. The recent investigations of Funke, Lehmann, and others have, however, shown that the substance which is associated with hæmatin in the blood-cells differs essentially from true globulin. It is sufficient here to indicate two leading points of difference. Globulin cannot be

Chemical constituents of the blood-cells.

Hæmatocrystallin.

* Charakteristik d. Epidem. Cholera, 1850, p. 33.

† Arch. d. Verein f. ges. Arb. vol. i. p. 161.

‡ Quoted by Henle in his Report on the Progress of Anatomy during the year 1855, in Canstatt's Jahresbericht. Würzburg, 1856, vol. i. p. 34.

obtained in a crystalline form, and is completely precipitated from its aqueous solution by a stream of carbonic acid, while the protein-body contained in the blood-cells is distinguished from all similar bodies by its crystallisability, and it is not precipitable by carbonic acid. The leading characteristics of this substance, to which the term *hæmatocrystallin* is applied, have been already described in p. 116. The moist blood-corpuscles contain from 18 to 26% of dry hæmatocrystallin, while its amount in the whole blood ranges from 9 to 12%.

Hæmatin.

The insoluble highly ferruginous hæmatin, which has been described in p. 94, does not occur in that condition in the blood, but is merely a product of the metamorphosis of the true blood-pigment. It occurs in the blood in a soluble form, and is so intimately associated with the hæmatocrystallin that it cannot be obtained in a pure condition in a soluble state. On the assumption that the soluble pigment existing in the cells contains the same amount of iron as the artificially prepared hæmatin, namely 6·93%, the blood-corpuscles of an adult man must contain 16 or 17% of this constituent.

There seems reason to believe that when there is an excess of water in the blood the hæmatin occurs in relatively greater quantity in the blood-corpuscles.

Fats.

A considerable quantity of the fatty matter contained in the blood is accumulated in the corpuscles, which in their dry state contain, according to Lehmann, from 2% to 3% of fat, consisting of a mixture of margarin, olein, margarate, oleate, and glycero-phosphate of potash, and cholesterin.

The cells in venous blood contain more fat than those in arterial blood.

Extractive matters.

The so-called extractive matters, whose chemical nature is still most imperfectly understood, occur in the blood-cells, although less abundantly than in the plasma. In the solid residue of the cells these extractive matters scarcely average 6%, while in the solid residue of the serum of the same blood they amount to about 8%.

In addition to acid phosphates or conjugated phosphoric acids, Lehmann infers that the blood-cells must likewise contain a nitrogenous non-crystallisable acid; for if the crystalline substance of the blood be coagulated by heat from its watery solution, the filtered fluid has an acid reaction, and, in addition to acid earthy phosphates, contains this acid whose characters are that it is not crystallisable, that it reddens litmus, that with bases it forms salts which are soluble in water and for the most part in alcohol, and that, on heating, it develops a gelatin-like odour and leaves a bulky carbonaceous residue difficult of combustion.

Salts.

We are indebted to the laborious and accurate investigations of Schmidt for a knowledge of the fact that the collective mineral constituents of the blood-cells are by no means identical with those which we find in the serum, although some salts are common (in different proportions) to both. He has discovered that the fluid of the blood-cells (that is to say, the water contained in the blood-corpuscles) contains, in addition to organic matters, a great preponderance of phosphates and potash salts, so that the phosphate of potash and the greater part of the chloride of potassium belong to the blood-cells, while the chloride of sodium, with a little chloride of potassium and phosphate of soda, belongs to the plasma. In the latter the organic matters are combined solely with soda, while in the blood-cells the fatty acids and the hæmato-globulin are associated with potash as well as with soda.

Preponderance of potassium and phosphoric acid

In analysing a specimen of blood which contained 396·24 of blood-cells and 603·76 of intercellular fluid, Schmidt found 1·353 of chloride of potassium and 0·835 of phosphate of potash in the former, and 3·417 of chloride of sodium, with 0·267 of phosphate of soda and 0·270 of chloride of potassium in the latter.

The following table, calculated for 100 parts of inorganic matters, gives the chief results of Schmidt's observations: —

| Genus. | Blood-cells. | | Plasma. | | Blood-cells. | | Plasma. | |
|---|---|---|---|---|---|---|---|---|
| | K. | Na. | K. | Na. | $PO_5$. | Cl. | $PO_5$. | Cl. |
| Man (Mean of 8 analyses). | 40·89 | 9·71 | 5·19 | 37·74 | 17·64 | 21·00 | 6·08 | 40·68 |
| Dog . . . | 6·05 | 36·17 | 3·25 | 39·68 | 22·12 | 24·88 | 6·65 | 37·31 |
| Cat . . . | 7·85 | 35·02 | 5·17 | 37·64 | 13·62 | 27·59 | 7·27 | 41·70 |
| Sheep . . . | 14·57 | 38·07 | 6·56 | 38·56 | 8·95 | 27·21 | 3·56 | 40·89 |
| Goat . . . | 14·98* | 37·41* | 3·55 | 37·89 | 9·41 | 31·73 | 5·90 | 40·41 |

These results have received further confirmation from Weber's† comparative analyses of the serum and of the clot of horses' blood, while they strengthen the view propounded several years ago by Nasse, that the phosphates are most abundant in the blood of those animals in which the corpuscles are most numerous (as in the pig, goose, and hen), and most scanty in those animals in which the opposite condition holds (as in the sheep and the goat), and that the phosphates are mainly contained in the corpuscles.

The differences between the salts of the blood-cells and of the plasma are most obvious in human blood; in the carnivora the difference is most distinctly seen in reference to the phosphoric acid, while in the herbivora it is most marked in reference to the potassium.

The corpuscles of arterial blood are invariably richer in salts than those of venous blood.

Earthy phosphates.

The earthy phosphates occur in the blood-cells in considerable quantity, although not so abundantly by about one-half as in the plasma; Schmidt found that in the former they amounted to 0·218 p. m., while in the latter they reached 0·550 p. m.

* In Schmidt's original table (Charakt. d. Epidem. Cholera, p. 14) these figures are reversed, but it is far more probable that there should be an accidental misplacement of the figures than that they should differ so enormously from the corresponding numbers in the sheep.

† Pogg. Ann., 1850, vol. lxxxi. pp. 99—115.

The iron of the blood pertains almost solely to the hæmatin of the blood-cells. The blood-corpuscles obtained from the hepatic veins contain less iron than those from the portal vein; and, according to Schmidt, there is an excess of iron in the blood-cells in hydræmic conditions of the system, whence he concludes that in these cases the cells have become poorer in hæmatocrystallin, and hence relatively richer in hæmatin.

In dry blood-corpuscles Schmidt found 0·4348% of iron in man, 0·509% in the ox, 0·448% in the pig, and 0·329% in the hen.

(197.) The gases of the blood, carbonic acid, nitrogen, and oxygen, are almost entirely contained in the blood-corpuscles, as is shown by the fact that whipped blood, which contains almost all the corpuscles, possesses a very considerable power of absorbing gases, while the serum scarcely absorbs more than water. It appears from the experiments of Magnus on the blood of the calf, the ox, and the horse, that defibrinated blood will absorb 1·5 times (or 150%) its own volume of carbonic acid, but only from 10 to 13% of its volume of oxygen, while it does not absorb more nitrogen than pure water. The combinations which these gases form with the constituents of the blood are somewhat unstable, as is obvious from the facts that the greater amount of the gas can be again extracted from the blood *in vacuo*, and that one kind of gas will expel another. Nitrogen occurs in nearly equal quantity in venous and in arterial blood, the amount ranging, according to Magnus, from 1·7 to 3·3% (by volume). In arterial blood there is relatively, but not positively, more oxygen than in venous blood; the ratio of the oxygen to the carbonic acid being as 6 : 16 in the former, and as 4 : 16 in the latter. The oxygen in the blood varies from 10 to 12·5% (Magnus), while the carbonic acid has been estimated at 66% in arterial and 78% (by volume) in venous blood (Magendie). Gases.

The view maintained by Magnus that the gases in question

enter into no chemical combination with the constituents of the blood either in passing to or from the tissues of the body, but form merely a physical mixture with the circulating fluid, is no longer generally accepted by chemists. If, for example, the oxygen were only mechanically absorbed and there were no chemical union, the blood could only take up the same quantity as an equal volume of water, namely 0·925%, whereas in reality it absorbs from 10 to 13%; and, further, the quantity of gases taken up would be proportional to the pressure, which is not the case. This greater force of absorption in the blood can only depend upon certain of its constituents, and principally, as we have shown, upon the corpuscles; only from 1-14th to 1-11th of the oxygen which is absorbed by the blood can be absorbed mechanically, that is to say, by the water, or can consequently exist free in the blood; the large amount of remaining oxygen (10-11ths at the lowest calculation) must be fixed by the blood-cells through the agency of some chemical attraction. Finally, in the main constituent of the blood-corpuscles, the hæmato-crystallin, we have an organic body which possesses a special affinity for these gases, and in which one gas can expel another.*

Unstable compounds of this nature are not very rare in chemistry. Carbonate of soda absorbs a considerable quantity of carbonic acid, forming the bicarbonate; and the same is the case with phosphate of soda; this carbonic acid may, however, be expelled either by another gas, as, for instance,

* For further and more detailed arguments in favour of the view advocated in the text—namely, that the absorbed oxygen, or the greater part of it, enters into chemical combination with one or more blood-constituents—I must refer to a long foot-note to p. 332 of Liebig's Letters on Chemistry, 3rd edition, 1851; to pp. 521—525 of the third volume of my translation of Lehmann's Physiological Chemistry, 1854; and to memoirs by Dr. Harley "On the Condition of the Oxygen absorbed into the Blood during Respiration," in Proc. Roy. Soc. for April 17th, 1856, and by Meyer "On the Gases of the Blood," in Phil. Mag. 1857, vol. xiv. pp. 263—268.

oxygen, or by greatly reducing the atmospheric pressure: and we have already pointed out (p. 115) that the globulin of the lens shares this property with these salts.

In further support of this view it may be urged that other gases, as, for instance, carbonic oxide, nitrous oxide, arseniuretted hydrogen, &c., exert an obvious chemical action on the corpuscles, when well agitated with the blood.

(198.) Before proceeding to the consideration of the intercellular fluid we must briefly notice other morphotic elements, which, in addition to the red corpuscles, are found suspended in the blood: these are the white or colourless corpuscles and the fibrinous flakes.

Colourless corpuscles.

It is now almost universally admitted that the colourless corpuscles of the blood are perfectly identical with the bodies occurring in lymph, chyle, mucus, and pus, to which the general term "cytoid corpuscles" has been applied. These corpuscles are nearly spherical (see *Plate V. fig.* 5), with a diameter of from ·004 to ·005″, and differ from the red corpuscles in not being elastic; their investing membrane is granular, and is always so viscid that the corpuscles possess a decided tendency to adhere in groups. The contents of these cells consist of an albuminous solution in which there are suspended extremely minute granules, together with a single, double, or triple nucleus, which may be either smooth or granular. Water causes the corpuscles to swell, and, by attenuating the cell-wall, renders the nucleus more visible; but the best method of exhibiting the nucleus distinctly is by the addition of acetic acid, which dissolves the cell-wall.

Ratio of the white to the red corpuscles.

We usually find it stated that the ratio of colourless to red corpuscles is about 1 : 10. It is, however, usually much below this. Donders and Moleschott* estimate it at 1 : 373, their results being based on the examination of blood from seven

* On this subject, see also Kölliker's Manual of Human Histology, translated by Busk and Huxley, vol. ii. p. 330, and Milne Edwards's Leçons sur la Physiologie et l'Anatomie Comparée, vol. i. p. 350.

individuals at different periods of life. They find moreover that food rich in albumen increases the quantity of the colourless cells, and that there is a similar excess during the periods of menstruation and of pregnancy.

The blood of the splenic vein is specially rich in these colourless cells (Funke), and the blood of the hepatic veins contains them more abundantly than that of the portal vein. They have been observed in excess after repeated venesections (Remak) and in cases of pneumonia and tuberculosis; and they are especially abundant in pyæmia and still more so in leucæmia, when they often stand to the red corpuscles in the ratio of 1 : 3.

Fibrinous flakes.

The so-called fibrinous flakes were originally discovered and named by H. Nasse.* The researches of Döderlein, Bruch, and others have, however, clearly shown that these flakes are not composed of fibrin. They seem chemically to resemble horny tissue, and are mostly epithelial cells, partly derived from the inner coat of the blood-vessels and partly (as Bruch maintains) from the face of the observer.

Constituents of the plasma.

(199.) The intercellular fluid or plasma contains the fibrin in solution as well as the constituents of the serum. We shall commence with the consideration of the fibrin, because in the first place, it is the most highly organised substance in the plasma; and secondly, because, from its separation from the blood, by spontaneous coagulation, in the clot, it is closely associated with the blood-corpuscles.

Fibrin.

(200.) The chemical characters of fibrin having been sufficiently described in an earlier part of the volume (see p. 109), we shall confine our remarks mainly to the subject of its coagulation.

Process of coagulation.

The form in which the fibrin coagulates can be best observed with the microscope when we place between the slide and cover-glass a drop of fluid free from blood-cells, ob-

* Müller's Archiv. 1841, p. 439.

tained from blood whose corpuscles have slightly sunk below the surface before it began to gelatinise. We first of all observe, scattered over the field, isolated molecular granules, from which extremely fine straight filaments very soon project, extending like rays from each point, but not forming regular star-like masses, such as we observe in certain crystals. These filaments become gradually elongated, and frequently cross one another, so as finally to resemble a tangled cobweb; and this net-work soon becomes so dense as almost to conceal the colourless corpuscles which are embedded in it. As fibrin, when we examine it in a drop of dried blood, exhibits a laminated appearance, many observers are of opinion that it separates in lamellæ during coagulation, and that the fibrous appearance is due solely to the duplication or overlapping of these lamellæ.

Cause of coagulation.

(201.) Chemists and physiologists have long endeavoured to ascertain the agency by which the fibrin is held in solution in the circulating blood, and the cause of its separation in a solid form in the blood that has been abstracted from the body. Until very recently (1856) the view generally adopted was that the oxygen of the atmospheric air induced such a change in the dissolved fibrin that it became insoluble in the alkaline plasma. The researches of Dr. Richardson have, however, shown that the presence of oxygen is not necessary to secure coagulation; in fact, that blood will coagulate as rapidly in the presence of nitrogen alone, of hydrogen, or other gas, as in the presence of oxygen, and more rapidly in a vacuum than under other circumstances. These observations are corroborated by reference to the experiments of Sir H. Davy, Dr. John Davy, and Sir C. Scudamore. Reasoning on these and other experiments, Dr. Richardson has come to the definite conclusion that coagulation is due to the escape of some volatile agent. This view had also been held by Scudamore and Polli, who imagined that carbonic acid gas was the eliminated principle. To put the question beyond

doubt, Dr. Richardson collected the vapour from a large quantity of blood, and then drove it through a small quantity of blood newly drawn into a test tube. So long as the blood-vapour was slowly passing through the blood, coagulation was suspended. Having settled the question thus far, this physiologist proceeded to examine what agents were evolved in the blood-vapour. He found carbonic acid gas and nitrogen were thus evolved; but on driving these gases through blood, they had no power in holding the blood fluid. They were, therefore, excluded from the argument. Something else had to be looked for. Remembering that the blood was alkaline, and that a salt of ammonia was present in blood, he sought for the volatile alkali in blood-vapour, and definitely found it. By holding a microscope glass moistened with pure hydrochloric acid over blood while coagulating, he obtained, on drying the glass, unmistakable crystals of hydrochlorate of ammonia. He also drove the vapour of blood through dilute hydrochloric acid, and by the chloride of platinum test obtained the crystals of the double salt of chloride of ammonium and platinum. Next, on adding ammonia, or neutral carbonate of ammonia, to blood, he discovered that newly drawn blood could be thus kept fluid for lengths of time, varying according to the amount of ammonia added, and to the conditions under which the blood was placed, *i. e.*, as regarded the possibility of an escape of ammonia, and the surrounding temperature. Finally, he succeeded in redissolving blood-clot in serum alkalinified with ammonia, and in re-inducing coagulation on gently driving off the volatile alkali.

The quantity of ammonia necessary to hold blood temporarily fluid is exceedingly small. Dr. Richardson computes that, in the living and healthy body, with the blood sealed up in its containing vessels and in steady motion, one part of ammonia is all-sufficient to sustain the fluidity of 3000 parts of blood, or even more.

The time of coagulation of healthy human blood varies according to external circumstances. At a temperature of 60°, the process is generally complete in three minutes. Below this point, the process is retarded; above, it is proportionally quickened.

In the dead body, if the death take place rapidly, if the blood at the moment of death is fluid, and if the circulatory system is entire, coagulation is often postponed for many hours, but occurs in a few minutes when the body is laid open, and the blood is exposed to the air.

Circumstances modifying the period of coagulation.

(202.) The period at which coagulation commences and is completed is modified by various physiological and pathological conditions. Strong agitation of the blood, whether by shaking or stirring, promotes the separation of the fibrin. The free access of atmospheric air or oxygen has the same effect, and hence blood coagulates more rapidly in flat and open than in deep and narrow vessels; for the same reason it coagulates more rapidly when it trickles slowly from a vein than when it flows in a full stream. Blood which is rich in carbonic acid coagulates less rapidly than when the contrary is the case; hence in cyanosis and in inflammatory disorders it is slow in coagulating. Blood containing an excess of water, or to which water has been added in small quantity, coagulates rapidly, while large quantities of water (more than twice the bulk of the blood) tend to retard coagulation; hence we find that, after repeated venesections and in anæmia, the blood coagulates more rapidly than in healthy persons. Little is known with accuracy regarding the action of salts on the coagulation, except that dilute solutions of the alkaline sulphates, nitrates, hydrochlorates, carbonates, and acetates, retard that process. As, in most of the experiments on this subject, no attention has been paid to the degree of dilution of the saline solution, or to the quantity of the solution employed, the results are of little value. Viscid solutions

of indifferent organic substances, such as albumen, casein, and sugar, retard the coagulation of the blood. The influence of temperature on the coagulation has not yet been sufficiently studied; we know, however, that, when blood is frozen before or during coagulation, it coagulates after thawing, just as if it had not been frozen. It appears very doubtful whether the quantity of fibrin exerts any influence on the period of coagulation. In the present imperfect state of our knowledge in reference to the blood, we are unable to explain why this fluid does not coagulate in the bodies of persons who have been struck by lightning, have been hanged, or who have died from asphyxia or narcotic poisoning, while it coagulates very rapidly in cases of plague, and after the infliction of venomous bites.

Consistence of the clot.

(203.) The consistence of the clot is liable to great variations, which, however, are not dependent, as was long supposed, on any peculiarities in the chemical composition of the fibrin, but upon certain mechanical influences, of which the most important is the relative quantities of the blood-corpuscles and of the fibrin. When the number of corpuscles is small in relation to the quantity of fibrin, the latter contracts more closely, and a dense firm clot is formed; while, if the corpuscles are much in excess, the fibrin seldom coagulates so firmly, and thus we have a soft friable clot. As the lower part of the clot contains an excess of corpuscles, it is always softer and looser in texture than the upper part. For a similar reason, the clot in the blood of plethoric persons is large and soft; while in that of chlorotic patients it is small and firm. An excess of water diminishes the consistence of the clot, as has been found both by direct experiments (the addition of water) and by observations on morbid hydræmic blood. Carbonic acid and salts which impede coagulation, give rise to a soft clot; thus, while highly oxygenised, bright red blood forms a dense elastic clot, the over-carbonised blood

of cyanotic and asphyxiated persons yields a very soft gelatinous coagulum.

(204.) The form of the clot mainly depends upon the shape of the vessel in which the coagulation of the blood takes place; although there are other modifying circumstances, amongst which we must especially mention the period of coagulation of the fibrin, and the sinking tendency of the blood-corpuscles. The clot is often observed to be covered on its surface with a thicker or thinner layer of tough fibrin (the buffy coat or inflammatory crust), concave in the centre, with a raised margin, presenting what is termed a cupped appearance. The appearance known as the buffy coat is caused by the corpuscles sinking below the surface of the fluid before the fibrin begins to separate and coagulate: from the absence of corpuscles at and near the surface, the fibrin, which in due time coagulates there, will be of a whitish grey colour, and will contract more firmly than the under portion in which corpuscles are embedded, and hence the cup-shaped depression with the raised margin. There are also various accessory conditions which favour the production of the buffy coat, as for instance—1. The form of the vessel in which the blood coagulates. In a high narrow vessel the corpuscles sooner sink below the level of the fluid than in a wide shallow one, and thus leave a part of the fibrin to coagulate without them; on this account, inflammatory blood is often found to yield no buffy coat in a flat vessel, whilst, on the other hand, blood which is considered of a non-inflammatory character often exhibits a buffy coat, if received in a narrow cylinder. 2. The number of corpuscles is not without influence. When the corpuscles are relatively few in number, and their sinking tendency is considerable, a buffy coat will be readily formed. On this account it is formed after repeated venesections, in anæmia, pregnancy, &c.* 3. An excess of fibrin was formerly regarded as the main cause of the formation of this coat; and

Form of the clot.

Buffy coat.

as the increase of fibrin was considered proportional to the progress of inflammation, this buffy coat received the name of the inflammatory crust. The quantity of fibrin doubtless exerts some influence on the thickness of the buffy coat; but that it is not the principal cause of this coat, is obvious from the fact that inflammatory blood which is very rich in fibrin often forms no crust, while blood that is poor in fibrin may in many chronic cases present it.

Hitherto we have assumed that the corpuscles have sunk rapidly, and that the fibrin has coagulated slowly. Sometimes, however, the converse relations are observed; and then we not only have no buffed or cupped appearance, but, in addition to a dense clot, we have a red sediment of corpuscles. Henle explains this by assuming that the fibrin coagulates and becomes contracted before the corpuscles had arranged themselves in the nummular form, and that, on the contraction of the gelatinised fibrin, a large number of the isolated corpuscles are expressed, which at first render the serum turbid and red, but soon deposit themselves in a sediment.

Quantity of fibrin in the blood.

(205.) The quantity of fibrin in the blood in various physiological and pathological conditions is sufficiently noticed in pp. 110, 237, 239, 240, and 244.

The serum.

(206.) The serum, after the separation of the fibrin and the blood-corpuscles, often contains certain undissolved particles in suspension, which communicate to it a milky or, at all events, an opalescent appearance. This turbidity of the serum has been observed in blood taken some hours after a meal; (Lehmann, however, failed to observe anything of this kind either in carnivorous or herbivorous animals;) it has likewise been noticed after prolonged fasting, during pregnancy, and very frequently, but not invariably, in the blood of drunkards. In these cases, the turbidity is due to the presence of suspended fat, as may readily be seen by a microscopic examination, or by shaking the serum with ether.

Its occasional turbidity.

A variety of turbid serum sometimes occurs in the blood in inflammatory conditions. The turbidity in this case depends upon the presence of very small dark molecules of a protein-body, supposed by Zimmermann to be a variety of fibrin, but regarded by Scherer and Lehmann as separated albumen. As in these cases the serum is only very faintly alkaline, and the turbidity disappears on the addition of a neutral alkali salt, it is most probable that the albuminate of soda in the blood has been deprived of some of its alkali, and that a portion of the albumen, thus freed from its soda, separates in the molecular form.

Quantity of water in it.

(207.) The quantity of water in the serum usually stands in a direct ratio to the quantity of water in the whole blood. All observers agree that the serum of woman's blood is more watery than that of man's blood. Schmidt, one of our most accurate chemists, found 90·884% of water in the latter, and 91·715% in the former. In pregnancy the serum is especially rich in water.

It is uncertain whether copious draughts of fluid occasion a temporary augmentation of water in the serum, in consequence of the rapidity with which an excess of water is removed from the blood; but there is no doubt that, in the absence of proper nourishment for any length of time, we have a diminution of the solid constituents of the serum, and consequently a relative increase of water. Since in most diseases comparatively little food is taken, and the nutritive function is commonly more or less impaired, the blood in these cases is, with a few exceptions, richer in water than in the normal state.

A decided and absolute diminution of the water in the serum and in the blood generally is only observed in cholera.

The serum of arterial blood is richer in water than that of venous blood. On comparing the blood of the temporal artery of a horse with that of the external jugular vein, Leh-

mann found that the relative quantities of water in 100 parts of serum were 89·333 and 86·222. The serum of the portal blood contains more water than that of any other venous blood, and in this respect differs remarkably from the blood of the hepatic veins.

The quantity of water in the serum is found to vary considerably in the blood of different animals — the serum of amphibians contains the largest amount of water, and that of birds a larger quantity than that of mammals.

Albumen. (208.) The most important constituent of the serum is albumen — the raw material from which all the other protein-bodies, and probably all the nitrogenous tissues of the animal body, are elaborated. Its quantity varies in healthy serum from 7·9 to 9·8%, and in the collective blood from 6·3 to 7·1%.

In most diseases, especially in scurvy, malaria, puerperal fever, dysentery, Bright's disease, and dropsy from organic disease of the heart or liver, the quantity of albumen in the serum is diminished; while in intermittent fevers, after drastic purgatives, and in cholera, it is increased.

Becquerel and Rodier believe that they have established the fact, that the transudation of albuminous fluids (or, in other words, dropsy) begins when the albumen in the serum sinks below 6%.

The process of digestion is accompanied by an augmentation of the albumen in the blood. Arterial blood contains less albumen than venous blood; while Lehmann found 11·428% of albumen in the venous blood-serum of the horse, he found only 9·217% in the corresponding arterial serum. Of venous blood, the portal blood is the poorest, and the hepatic blood the richest, in albumen. Human blood contains rather more albumen than that of most mammals.

Casein. (209.) Many observers (Panum, Moleschott, Stas, &c.) regard casein as a normal constituent of the serum, and

maintain that it is especially abundant in the blood during pregnancy, and in the puerperal state. There can be no doubt that a substance strongly resembling casein does occur in the serum, and has even been determined quantitatively (see p. 114); but as we have already shown (p. 106), certain modifications of albumen can hardly be distinguished from casein.

(210.) The fat contained in the serum consists chiefly of stearates, margarates, and oleates, with a little cholesterin: the serolin, which was formerly supposed to occur there, being apparently only a mixture of the crystallisable parts of the above fats. The phosphorised fats which (as has been already mentioned) are found in the corpuscles, do not occur in the serum. The quantity of fat in the normal serum is very variable, but about 0·2% seems to be the average quantity. During digestion the quantity of fat in the serum is increased. The blood-serum of women usually contains more fat than that of men. The serum of arterial blood contains less fat than that of venous blood, the relative numbers in the case of the horse being, according to Lehmann, 0·264% and 0·393%. The greatest quantity of fat is found in the serum of the portal blood; while that of the hepatic veins contains less than that of the portal blood, but much more than the serum of jugular blood. Fats.

From the investigations of Becquerel and Rodier it appears that the quantity of fat, and especially of cholesterin, is increased at the beginning of every acute disease; it is likewise increased in chronic affections of the liver, in Bright's disease, in tuberculosis, and in cholera.

(211.) The extractive matters of the serum are formed by a mixture of various known and unknown organic bodies. Their amount is liable to great fluctuations, ranging, according to Lehmann, from 0·25 to 0·42%, and when we consider how many things are vaguely included in this Extractive matters.

term, and how their amount must in a great measure vary with the rapidity of the metamorphosis of the tissues, we need not be surprised at the irregularity of their quantity. Nasse has found more extractive matters in the blood of children and young animals than in the blood of adults—an observation which accords with what Scherer has noticed in the urine. Arterial blood contains more extractive matters than venous blood. Of venous blood, that of the hepatic veins contains more than that of the portal vein, and the latter more than that of the jugular.

The only diseases in which the extractive matters have been observed to be much increased are puerperal fever and scurvy.

We have recently succeeded in detecting (in small quanties) various known substances which formerly passed unrecognised among the extractive matters: these are sugar (see p. 88), urea * (see p. 46), creatine (see p. 36), creatinine (see p. 37), hypoxanthine in the blood of the splenic vein (see p. 50), hippuric acid (see p. 59), and probably formic, acetic, and lactic acids (see pp. 11, 21). (That formic and lactic acids exist in the blood seems obvious from the fact that the sweat contains an abundance of the former and the muscles of the latter. All three acids have moreover been found in the blood of the splenic vein.) There is also an odorous

* The researches of M. Picard on the determination of the urea in the blood are briefly alluded to in a note to p. 46. Since the sheet containing that note was printed, I have obtained fuller information regarding his investigations on this point. The following are some of the results. In the blood of healthy men he found 0·0177%, 0·0142%, and 0·0165% of urea; and in that of healthy women, 0·0153% and 0·0169% The blood of a woman in the sixth month of pregnancy contained 0·0260%, that of a woman at the ninth month 0·0113%; and that of a woman two days after delivery 0·0187%. The blood of a man who had fasted for some time contained 0·0177%, and five hours after a meal of animal food, 0·0175%. Placental blood contained 0·062%, 0·028%, and 0·027%. The blood of the carotid artery of a horse contained 0·0293%, while that of the external jugular vein contained 0·035%.

principle which has not yet been isolated, but which is probably a volatile fatty acid; the odour which is very characteristic in the blood of some animals (as, for instance, the goat, the sheep, and the cat) is most distinctly developed when we mix the blood with rather more than its volume of sulphuric acid (see p. 201).

In different varieties of morbid blood we not only find in the extractive matters certain of the above-named substances in excess, but likewise bile-pigment and the biliary acids (sometimes even when there is no apparent disease of the liver), hypoxanthine and glutin (in leucæmic blood), and oxalic and uric acids in gout (see p. 67).

Mineral constituents.

(212.) It appears from the best analyses which we possess of the ash of the serum, that it is composed of:—

| | |
|---|---|
| Chloride of sodium . . . . . | 61·087 |
| Chloride of potassium . . . . . | 4·054 |
| Carbonate of soda . . . . . | 28·880 |
| Phosphate of soda ($2NaO,PO_5$) . . . | 3·195 |
| Sulphate of potash . . . . . | 2·784 |
| | 100·000 |

The sulphate of potash in the above table is a product of incineration, and so probably to a considerable extent is the carbonate of soda. The blood-serum of man contains rather more salts than that of woman (the relative numbers having been estimated at 8·8% and 8·1%), and that of adults more than that of children.

From the examination of the blood of different kinds of animals living on food of the most opposite character, it appears that the nature of the diet does not materially affect the amount of the saline constituents. The investigations of Nasse and Poggiale show that the blood of cats, goats, sheep, and calves contains the most salts, then that of birds, then that of man and the pig; while the blood of dogs and rabbits

contains the smallest quantity. The prolonged use of an excess of salt seems, however, to render the blood richer in chloride of sodium.*

Arterial serum is somewhat richer in salts than venous serum, if we except the serum of the portal blood. After prolonged or repeated venesection, the blood which is drawn last contains more salts than that which first escapes.

In severe inflammatory affections, and especially in cholera, the saline constituents of the serum are much diminished; while in the acute exanthemata, in typhus, dysentery, malignant intermittent fevers, scurvy, Bright's disease, and in all varieties of dropsy and hydræmia, they are considerably increased.

Silica has hitherto only been detected in the blood of birds; but that it must occur in minute quantity in the blood of man and other mammals, seems evident from the fact that it is a constituent of the hair.

Carbonate of ammonia is commonly supposed only to exist in the blood in typhus and other diseases of a low type, in cholera, and in those disorders in which urea accumulates in the blood.

(213.) We now proceed to notice the differences which the blood presents in its chemical composition under various physiological conditions.

Influence of sex on the blood.

The blood of women is of rather a lighter tint than that of man, is of lower specific gravity, developes a less intense odour of sweat on the addition of sulphuric acid (see p. 201), and contains more water and fewer blood-corpuscles; as there is a preponderance of serum in female blood, the latter contains more albumen, fats, and extractive matters than male

* Plouviez took daily 10 grammes (about 2·5 drachms) of salt with his food for three months. At the commencement of the experiment the salt in 1000 parts of his blood amounted to 9·33, of which 4·40 were chloride of sodium; while at the conclusion they amounted to 11·84, of which 6·10 were chloride of sodium. (Compt. rend., 1847, vol. xxv. pp. 110—113.)

blood; although the serum of female blood contains less salts than that of male blood, the actual blood contains more salts in the female than in the male sex. (See Tables in pp. 206, 207.)

In pregnancy*, the blood is usually of a darker colour than in the non-pregnant state; it has a low specific gravity, being rich in water, and deficient in red corpuscles; the fibrin is relatively increased, which accounts for the small compact clot and the buffy coat which are often observed during pregnancy. The serum contains less than the normal quantity of albumen; but the casein-like substance is found in augmented quantity in the serum towards the end of pregnancy and in the puerperal state. (See p. 114.) Of pregnancy.

The blood of young children is richer in solid constituents, especially in red corpuscles and extractive matters, but poorer in fibrin and salts, than the blood of adults. Of age.

In advanced age, and in the female sex, from the period when menstruation ceases, the blood becomes relatively poor both in red corpuscles and albumen; the cholesterin is, however, somewhat increased (Becquerel and Rodier).

During digestion the blood becomes richer in solid constituents; there is a marked augmentation of the colourless corpuscles, and a slight excess of red corpuscles, albumen, fat, and salts; the fibrin is slower than usual in coagulating; and, from the excess of fat, the serum is not unfrequently turbid. Of digestion.

Prolonged starvation, depraved nutrition, and excessive loss of the animal fluids, produce very similar effects on the blood; the corpuscles are diminished, while the plasma be-

* Nasse, who has examined the blood of thirty-six women during the last three months of pregnancy, arrives at the following conclusions. The blood of pregnant women differs from that of women in the non-pregnant state, (1.) in its lower specific gravity (and this applies equally to the serum); (2.) in its containing more than the normal quantity of fibrin; (3.) in its exhibiting in more than three-fourths of the cases a buffy coat; and (4.) in the number of lymph-corpuscles being often much increased. (Arch. des Vereins f. gemeinsch. Arb., 1854, vol. i. pp. 351—373.)

comes more watery, and poorer in albumen and other organic constituents, but richer in salts. We are indebted to C. Schmidt* for the discovery of the important law, that *the diminution of albumen in the blood is always associated with a corresponding augmentation of salts.*

Difference between arterial blood and the blood of the larger and smaller veins.

(214.) The composition of the blood varies considerably, according to the part of the circulating system from which that fluid is obtained. Lehmann† has recently investigated this subject more fully than any preceding chemist, and we shall endeavour to extract from his memoir his most important conclusions, and to incorporate them with the results previously known.

From a very elaborate table, containing the numerical results of fourteen analyses of the blood of five horses — the blood of various veins (the external abdominal, the cephalic, the digital, and the jugular veins, and the inferior vena cava) being contrasted with the arterial blood of the same animal — he draws the following inferences: —

(*a.*) No definite conclusion could be drawn from the relative proportions of the serum and the clot; indeed, no inference could ever be deduced regarding the relative degrees of con-

* Charakteristik der Epidem. Cholera, Leipzig, 1850, p. 108.

† Untersuchungen über die Constitution des Bluts verschiedener Gefässe und den Zuckergehalt derselben insbesondere, in the Ber. d. k. Sächs. Ges. d. Wiss. zu Leipzig. Math. Phys. Classe, 1855, pp. 87—122. The main points discussed in this elaborate memoir are, (1.) On the differences of the blood of different veins as compared with arterial blood, based on fourteen analyses of horses' blood; (2.) On the quantity of sugar in the blood of different vessels; (3.) Comparative analyses of the blood of the hepatic and portal veins of dogs fed on animal diet; (4.) On the relative quantities of fat in the blood of the hepatic and portal veins; (5.) On the quantity of sugar in the blood of the hepatic and portal veins of dogs in various physiological conditions; (6.) On the sugar that has been assumed (by Figuier) to exist in the blood of the portal vein after an animal diet; (7.) On the chemical composition of various parts of the blood collected from the portal vein; and (8.) Do either the portal blood or the contents of the stomach or intestine contain any substance, after the use of an animal diet, that can by any known methods be readily converted into sugar?

tractility of the clot, because the blood, even though obtained as rapidly as possible after the death of the animal, occurred in a gelatinous or semi-coagulated state.

(*b.*) On comparing the fibrin of the blood of the *smaller veins* with that of arterial blood, we find it more abundant (in the ratio of 6 or even 6·5 $\frac{0}{00}$ to 4 $\frac{0}{00}$)* in the venous than in the arterial blood. If we might draw a conclusion from so small a number of cases, it would be that the fibrin is chiefly formed in the capillary system; we must, however, not overlook the fact, that in consequence of the diminution of the number of corpuscles in the capillaries the augmentation of the fibrin is in part only a relative one.

(*c.*) Two analyses of the blood of the *jugular vein* lead us merely to the unsatisfactory conclusion that this blood either differs in no material respect from arterial blood, or that it is liable to very considerable fluctuations in its composition.

(*d.*) The blood of the *vena cava* was examined three times, twice before the hepatic veins had poured their contents into it. Even in these two last cases, before it had been mixed with the non-fibrinous blood of the hepatic veins, its quantity of fibrin, as compared with that of arterial blood, was very small, being in about the ratio of 1 to 2 — a result that is the more striking, in consequence of the richness of the blood of the small veins in fibrin. The most probable explanation is, that the fibrin is mainly formed in the blood in its course through the arteries, that its quantity is considerably increased in the capillaries, where there is still an abundance of oxygen, and that it finally undergoes disintegration in the larger veins.

(*e.*) If we compare the *solid residue* of the serum of these different kinds of blood, we find that in the case of the vena cava there was, on an average, an excess of solid constituents,

* By the symbol $\frac{0}{00}$ we indicate "per mille."

and that in the jugular and the smaller veins there was a diminution, as compared with arterial serum. The quantity of *salts* in the serum of arterial blood is almost always greater than that in venous serum, but the augmentation is only relative, being due to the decomposition and disintegration of organic materials in the lungs. Although it is principally the extractive matters which undergo this fate, a portion of the albumen also disappears in the passage of the blood through the lungs, and is probably converted into fibrin and other substances. (On an average we find 2% less of albumen in the solid residue of arterial serum than in that of venous serum.)

(*f.*) The relative quantities of water and of the blood-corpuscles in the different kinds of blood were found by Lehmann to yield an additional confirmation of the law established by Becquerel and Rodier, that the amount of water in the blood usually stands in an inverse ratio to the quantity of corpuscles. The blood of the smaller veins constantly yielded more water and fewer corpuscles (on an average about 6% of each) than arterial blood; similarly, in the blood of the vena cava behind the openings of the hepatic veins there were found less corpuscles by about 2% than in arterial blood; and it was only in the case in which the blood was drawn from the thoracic portion of that vein that it was found to be richer in blood-cells than arterial blood (in the ratio of 13·9 to 8·2)—a result in complete accordance with the fact previously established by Lehmann *, that the blood of the hepatic veins is richer in corpuscles than that of any other vessel.

Portal blood.

(215.) Portal blood is very much influenced in its composition by the digestive process. During digestion, especially

* Einige vergleichende Analysen des Blutes der Pfortaden und der Lebervenen, in the Ber. d. k. Sächs. Ges. d. Wiss. zu Leipzig. Math. Phys. Classe, 1851, p. 131.

if the animal has been drinking, it is rich in water and intercellular fluid and poor in corpuscles; while the fibrin is slightly augmented, the albumen, extractive matters, and salts are moderately increased, and the fat still more so: the fibrin at this period presents no peculiarities, but when digestion is not going on, it possesses very slight contractility and forms an exceedingly friable clot.

As compared with the blood of the jugular vein, the portal blood is poor in blood-cells and in solid constituents generally. The cells are commonly described as irregular in shape, and appearing as if they were undergoing disintegration. In his latest memoir * on this subject, Lehmann, however, expressly states that neither in the portal blood of the horse nor of the dog could he detect any abnormality in the form of the red corpuscles, and that they in no way differed from the corpuscles of the jugular or other veins: moreover, he found colourless corpuscles in the blood of both these animals (the existence of which in portal blood was denied by Simon †), and in both these points he is confirmed by Funke.‡ The blood-corpuscles are richer in hæmatin and poorer in hæmatoglobulin than those of jugular blood, and contain double the amount of fat. The quantity of fibrin is much smaller, but it presents no peculiar quality except that it contains an excess of fat. Further, the albumen of the serum is much diminished, but there is an augmentation of the fat, extractive matters, and salts. No sugar is present unless the animal has been living on amylaceous food, when it is found in very small quantity.§

* Ber. d. k. Sächs. Ges. d. Wiss. Math. Phys. Classe, 1855, p. 99.

† Animal Chemistry with reference to the Physiology and Pathology of Man. London, 1845 (Printed for the Sydenham Society), vol. i. p. 202.

‡ Funke's edition of Wagner's Lehrbuch d. speciellen Physiologie. Leipz. 1854. p. 104.

§ In two dogs fed for two days on boiled potatoes, Lehmann only found traces of sugar in 100 parts of the solid residue of the portal blood; while in

Blood of the hepatic veins.

(216). The blood of the hepatic veins contains far more solid constituents than that of the portal vein or any other vessel. (In the case of three dogs whose portal and hepatic blood was analysed by Lehmann, the latter was on an average 6·3% richer in solid constituents than the former.) It is remarkably rich in corpuscles, both white and red, exceeding the portal blood in this respect by more than 6%. The white corpuscles occur in various forms and sizes. The red cells collect in groups of a distinct violet colour, and present a greater resistance to the action of water than the corpuscles of any other blood: they are poorer in hæmatin (or at all events in iron, the iron of the solid residue of the clot being to that of portal blood in the average ratio of 35 to 22) and in fat, but richer in extractive matters. The intercellular fluid of this blood contains no fibrin (consequently there is no coagulation), less albumen and fat, and far less salts than the blood of any other vessel; but it contains such an excess of extractive matters that its solid constituents exceed those of any other blood. This blood is likewise distinguished for the abundance of sugar which it contains. This sugar, which is formed in the liver, gradually diminishes with the distance from the point of opening of the hepatic veins into the vena cava till it finally disappears, under ordinary circumstances, in the pulmonary circulation.

Blood of the splenic vein.

(217.) In its microscopical characters the blood of the splenic vein closely resembles that of the hepatic veins. Funke,* who has carefully examined this blood in the horse, the dog, the ox, and in man, states that the red corpuscles in these two kinds of blood resemble each other in their minuteness, in their more than usually spherical shape, in their

two horses fed on bran, hay, and straw the quantities were 0·055 and 0·0052 respectively. Poggiale, however, finds a larger amount of sugar in the portal blood of animals fed on amylaceous food. (See Bernard's "Leçons de Physiologie," &c. Paris, 1855, vol. i. p. 498.)

* Op. cit. p. 117.

accumulating in heaps, and not assuming the nummular arrangement, and in the resistance which most of them offer to the destructive action of water, and some even to the action of acetic acid. The colourless cells are very abundant, often even more so than in hepatic blood, sometimes amounting to one-fourth of the total number: they do not lie uniformly scattered over the field, but are accumulated in large round heaps, which often enclose red cells; on the addition of acetic acid the presence of one or more nuclei is often revealed. Granular cells are not unfrequently seen in this blood, especially in horses; and blood-corpuscle-containing cells have been often seen in it by Kölliker and Ecker *, occasionally by Mr. Gray, and once by Funke. In addition to the above varieties of cells, Mr. Gray directs attention to the almost constant existence of numerous pigment granules, or masses, or rod-shaped crystals, which either exist free or are contained in cells. The pigment granules are of a dark black or dark reddish brown colour, while the rod-like bodies are of a red or yellowish red colour.

The red cells of the blood are remarkable for the facility with which their contents crystallise; it is only necessary to allow splenic venous blood to stand exposed to the air and to light to obtain the crystals described in p. 116; it was thus that Funke made his discovery of hæmatocrystallin.

The only analyses of the blood of the splenic vein are those of Beclard, Funke†, and Gray.‡ The chief point established by Beclard's analyses is that the blood of the splenic vein contains less blood-corpuscles than that of other veins. Funke's researches by no means confirm Beclard's view. The main difference detected by him between the blood entering and leaving the spleen is that the latter is

* Zeitsch. f. rat. Med. vol. vi. p. 261.

† Ib. (New Series), vol. i. pp. 172—218.

‡ On the Structure and Uses of the Spleen. London, 1854, p. 147.

always considerably poorer in fibrin than the former, there often being hardly any traces of this substance in the blood of the splenic vein; moreover, a small portion of the salts which had belonged to the blood-cells was always found in the intercellular fluid. The results obtained by Mr. Gray from a very large number of analyses of horses' blood, show that the blood emerging from the spleen presents the following marked and constant peculiarities. It contains less solid matter than arterial or other venous blood, the solid residue in 1000 parts of splenic venous blood being to that in the same quantity of arterial blood as 187·1 to 239. It contains far less blood-globules; while the average amount (the mean of ten experiments) was $88{\cdot}5\frac{0}{0\,0}$, the corresponding amount in arterial blood was $162{\cdot}2\frac{0}{0\,0}$; the greatest diminution of the blood-corpuscles occurred about sixteen hours after the digestion of food, when the amount was only $27{\cdot}93\frac{0}{0\,0}$, while during digestion the amount was above $100\frac{0}{0\,0}$. The average amount of fibrin in splenic venous blood is double that of arterial blood; while the former contains $6{\cdot}4\frac{0}{0\,0}$, the latter only contains 2·26; and the fat is fully as much or rather more augmented. The albumen is increased; in ten experiments on this blood the average amount of this substance was $60\frac{0}{0\,0}$, while in arterial blood it was only $37{\cdot}2\frac{0}{0\,0}$. The amount of iron which is contained in the blood emerging from the spleen is considerably increased as compared either with arterial or jugular venous blood, and this is an important fact in connexion with the diminution of the number of the red corpuscles in the same blood. Lastly, a highly important peculiarity is the deep reddish brown colour of the serum, which depends upon the large amount of free hæmatin contained in solution.

Scherer* has analysed the parenchymatous juice of the

* Verhand. d. phys.-med. Ges. zu Würzburg, 1852, vol. ii. p. 298.

spleen, which obviously must consist chiefly of blood, with an admixture of lymph and of the fluid permeating the trabecular tissue and the coats of the vessels. He found in it a new nitrogenous crystallisable body, which he named lienine (but which he has since discovered to be identical with leucose), hypoxanthine, an albuminous body rich in iron, a large quantity of iron in combination apparently with acetic and lactic acids, highly carboniferous pigments very similar to those occurring in the urine and muscular juice, and uric, lactic, acetic, formic, and butyric acids. In consequence of this investigation, Funke sought for hypoxanthine and uric acids in the blood of the splenic vein; he failed, however, to detect any traces of either of these bodies *, nor did he find either pigment or iron in the serum.

Menstrual blood.

(218.) Menstrual blood contains no true fibrin; it separates into a colourless alkaline serum and a red sediment of blood-corpuscles, intermixed with which are numerous colourless cells. It contains about 16% of solid constituents. †

Placental blood.

(219.) The blood of the placental vessels contains, according to Stas ‡, a deficiency of albumen and fibrin, but a great excess of serum-casein; it is stated also to contain an appreciable quantity of urea (see note to p. 232).

Influence of venesection.

(220.) Repeated venesections diminish the specific gravity of the blood, render its colour lighter, cause it to coagulate earlier, but not so firmly as in the natural state, diminish the red corpuscles, and at the same time render them relatively

* Although we shall advert more fully to the subject in treating of the glandular juices, we may here mention that Mr. Gray (and his colleague, Dr. Noad, who materially assisted him in his analyses) failed in ever detecting either hypoxanthine or uric acid in the juice of the spleen; while Cloetta, and subsequently Gorup-Besanez (Ann. d. Ch. u. Pharm. 1856, vol. xcviii. p. 24), found both these substances in addition to the other bodies mentioned by Scherer.

† Various analyses of menstrual blood and of the lochial discharge are recorded in my translation of Simon's "Animal Chemistry," vol. i. pp. 337–339.

‡ Compt. rend. vol. xxxi. p. 630.

poor in hæmatocrystallin, and increase the water and colourless corpuscles to a considerable extent, while the fibrin is apparently unaffected.*

Blood in different diseases.

(221.) We shall confine our remarks on the condition of the blood in different diseases to those cases in which well-marked peculiarities of composition are manifested.

Inflammatory diseases.

In inflammatory diseases, especially when they are accompanied by general febrile excitement, we always have a greater or lesser augmentation of the fibrin, the increase varying with the degree and duration of the inflammation; the fibrin reaches its maximum † in pneumonia and acute articular rheumatism. At the same time there is usually, but not in-

* The following table, quoted in p. 249. of the first volume of my translation of Simon's "Animal Chemistry," fully bears out the statement made in the text: —

*Mean Composition of the Blood of Ten Persons bled Three Times.*

| | 1st Venesection. | 2d Venesection. | 3d Venesection. |
|---|---|---|---|
| Density of defibrinated blood - | 1056·0 | 1053·0 | 1049·6 |
| Water - - - - - | 793·0 | 807·7 | 833·1 |
| Solid constituents - - - | 207·0 | 192·3 | 176·9 |
| Fibrin - - - - | 3·5 | 3·8 | 3·4 |
| Blood-corpuscles - - - | 129·2 | 116·3 | 99·2 |
| Albumen - - - - | 65·0 | 63·7 | 64·6 |
| Extractive matters and salts - | 7·7 | 6·9 | 8·0 |
| Fat - - - - - - | 1·66 | 1·58 | 1·53 |

† The highest amount of fibrin ever observed by Andral and Gavarret, in their numerous analyses of morbid blood, was $10{\cdot}5\frac{0}{00}$, and the largest quantity ever found by Simon was $9{\cdot}15\frac{0}{00}$; Rindskopf and Scherer found this constituent amount to $12{\cdot}726\frac{0}{00}$ (Simon's "Animal Chemistry," vol. i. pp. 262, 265). In all these cases the disease was pneumonia. In acute rheumatism Andral and Gavarret once found $10{\cdot}2\frac{0}{00}$ in the blood. The following table shows the mean amount of fibrin in the blood in various inflammatory diseases, as determined by Becquerel and Rodier. (See their "Traité de Chimie Pathologique," Paris, 1854, p. 105.)

| | |
|---|---|
| The normal quantity of fibrin in health being . . . . | 2·5 |
| Its quantity in acute bronchitis is . . . . . | 4·8 |
| „ in acute pleurisy . . . . . | 6·1 |
| „ in acute pneumonia { first bleeding . . . | 7·4 |
| „ in acute pneumonia { second bleeding . . . | 6 8 |
| „ in acute articular rheumatism . . . . | 5·8 |

variably, a slight diminution of the blood-cells.* The albumen of the serum is diminished †, especially when there is much exudation. The salts are slightly diminished, and the fats (especially the cholesterin) somewhat increased.

Is there any connexion between the augmentation of the fibrin and the diminution of the corpuscles? Simon believed that the fibrin is the result of a special transformation of the corpuscles; and the circulation being accelerated in inflammatory diseases, the globules are exposed more frequently than in the normal state to the action of the oxygen in the lungs, and that an excessive production of fibrin in a given time was the result. The most powerful argument against this view is that no such augmentation of the fibrin occurs when we have accelerated circulation without inflammation, as in fever.

Another and more probable theory is that the augmentation of fibrin is due to an excessive transformation of albumen into fibrin — a view which is supported by the fact that the augmentation of the former corresponds pretty nearly, in a numerical point of view, with the diminution of the latter (see the Table in last page).

Andral and Gavarret, and subsequently Becquerel and Rodier, have made numerous analyses of the blood in typhoid and typhus fevers, as well as in simple continuous fever; it does not, however, appear that the blood in these cases pre- Fevers.

* Becquerel and Rodier, who fix the normal quantity of blood-cells at 132‰, their physiological limits being 145 and 125, find that in the inflammatory diseases mentioned in the preceding note the mean quantity of corpuscles was 123·3.

† The normal quantity of albumen in 1000 parts of normal serum being, according to these observers, 80, they found that the mean quantity in twenty cases of inflammatory disease (first bleeding) was 73·35; and in ten cases of second bleeding, 64·84.

sents any very well marked constant deviations from the normal type.

Cholera. In cholera the blood has a very high specific gravity *, and is remarkably tough and viscid: the corpuscles are increased in number, but are abnormally poor in salts; the amount of fibrin is unaffected; the serum is very dense, being extremely rich in albumen and containing more potash-salts and phosphates (though less salts collectively) than normal serum; it moreover usually contains some urea, together with an extractive matter, which seems to act as a ferment and to convert the urea very rapidly into carbonate of ammonia.

Dysentery. In dysentery the number of corpuscles is diminished; the fibrin is sometimes, but not always, increased; the solid constituents of the serum, and especially the albumen, are diminished, while the salts are increased.

Bright's disease. In Bright's disease the blood is impoverished, both in relation to the corpuscles and to the solid constituents of the serum; the cholesterin and the salts of the serum are however increased. Urea, either in mere traces or in very appreciable quantity, may be almost always recognised in the solid residue of the serum, and we sometimes can detect carbonate of ammonia as a product of its decomposition.

Plethora. In the condition known as plethora, the corpuscles are always somewhat augmented; the fibrin is unaffected, and the albumen of the serum is slightly above the average.

Anæmia and hydræmia. In true anæmia (by which we understand a deficiency in the quantity of circulating fluid) the blood exhibits no peculiarities of composition. The term anæmia is, however, often incorrectly used to signify hydræmia, which is a frequent concomitant of dropsy. The blood here occurs as a very

* The blood in cholera has been carefully examined by Schmidt (Charakteristik d. Epidem. Cholera, 1850). While in healthy men the specific gravity is 1·0599, the mean specific gravity in male patients with cholera was 1·0701; and, similarly, in female patients it was 1·062, the healthy specific gravity being 1·0503.

attenuated, pale, watery fluid, and in coagulating it forms a loose, infiltrated, gelatinous clot. Its composition is the same as in Bright's disease, except that there is usually no excess of urea.

Chlorosis.

In chlorosis the blood forms a small firm clot, floating on a large quantity of clear serum, and often covered with a buffy coat. The corpuscles, and consequently the iron, are always diminished, often to an extraordinary degree. Becquerel and Rodier found that while the mean normal amount of corpuscles in woman's blood was $127\frac{0}{00}$, the mean amount in chlorosis was 86·83, and they once found the number as low as 45·38). The composition of the plasma is usually normal.

Typhus.

In typhus (the abdominal form), during the first week, the composition of the blood closely resembles the condition of that fluid in plethora, and there is likewise a slight augmentation of the fibrin; but from about the ninth day the corpuscles and the solid residue of the serum begin to diminish, and continue to do so with a rapidity proportional to the intensity of the intestinal affection.

Puerperal fever.

The blood in puerperal fever has been carefully examined by several chemists, whose results are somewhat discordant. There is a considerable diminution of the corpuscles, and corresponding augmentation of fibrin (especially if there is much peritonitis), but it is soft and gelatinous; and there is almost always a buffy coat. In most cases, but not invariably, the collective solid constituents of the serum are much diminished, while the extractive matters are considerably increased. Bile-pigment and free lactic acid have been found in the serum.

Pyæmia.

We know nothing of the state of the blood in pyæmia, except that the fibrin is diminished and that there is a great augmentation of the colourless corpuscles.

Leucæmia.

The blood in leucæmia — an affection which is usually accompanied by a considerable enlargement of the spleen —

presents in many respects a close resemblance to the blood of the splenic vein. Scherer * has made two examinations of leucæmic blood, in each case obtained from the body after death; and the results are so remarkable that we shall give them somewhat fully.

In neither case did the blood spontaneously coagulate in a thorough manner: it merely formed a gelatinous semi-coagulated thick mass, whose surface was at first blackish, but, on exposure to the air, soon became more or less red, thus giving to the whole mass a black and red marbled appearance. In the first case the blood had a faintly acid reaction, perfectly coagulated when boiled with water, and the filtrate was found to contain many remarkable substances that do not commonly occur in the blood, namely—

(1.) Glutin, or a substance closely allied to it.

(2.) A peculiar organic matter, forming an intermediate link between the albuminous bodies and glutin.

(3.) Hypoxanthine to the amount of 8 or 10 grains in 4 ounces of blood. (The substance was previously discovered by Scherer in the spleen, and traces of it have been found in the normal blood of oxen. (See page 50.)

(4.) Formic, acetic, and lactic acids.

In the second case the blood did not coagulate so perfectly on boiling, and the filtrate did not exhibit the slightest tendency to gelatinise; hence the glutin found in the first case was here absent. The following substances, pertaining to the splenic juice, were however detected in the filtrate: hypoxanthine, leucine (which was not looked for in the first case), and uric, lactic, and formic acids.

The character from which leucæmic blood derives its name is due to the great excess of colourless corpuscles.

Carcinoma. The condition of the blood in carcinoma has been examined by several chemists (amongst whom we may mention Gorup-

* Verhandl. d. phys.-med. Gesellsch. zu Würzburg, 1852, vol. ii. pp. 321—325: and 1856, vol. vii. pp. 123—126.

Besanez*) who concur in the opinion that there is a great excess of fibrin even when no febrile symptoms are present. Lehmann seems to doubt whether this substance, which is found in such excess, actually is true fibrin. There is also a slight diminution of the corpuscles.

In diabetes the blood, except that it contains an excess of sugar, scarcely differs from the normal type. Diabetes.

(222.) Numerous analyses of the blood of various animals (mammals, birds, reptiles, and fishes) have been made by Andral, Gavarret, and Delafond, by Dumas and Prevost, by Simon, and by Nasse, and the results obtained by these chemists are recorded at considerable length in my translation of Simon's "Animal Chemistry."† Blood of various kinds of animals.

Amongst mammals we find that the blood of omnivorous animals (as the pig) contains more corpuscles (and consequently more iron and phosphates), more fibrin, and more collective solid residue of the serum, but less salts, than the blood of other animals. The blood of carnivorous animals presents nearly as many corpuscles as that of omnivorous animals, but as compared with herbivorous animals it contains less fibrin and more fat.

The blood of birds is as rich in corpuscles as that of omnivorous animals, and contains more fibrin and fat, but less albumen than that of most mammals.

In all the cold-blooded animals (reptiles and fishes) the blood is poorer in corpuscles and richer in water than in mammals or birds.

Notices of the blood of various molluscs and of insects may be found in Lehmann's "Physiological Chemistry."‡

(223.) The quantity of blood in the living body can only Quantity of blood in the body.

* Arch. f. Physiol. Heilk. vol. viii. pp. 523—525.

† Vol. i. pp. 339—350. The reader who wishes for further information on the blood of the domestic animals may be referred to Colin's Traité de Physiologie Comparée des Animaux Domestiques, Paris, 1856, vol. ii. pp. 174—184, which, however, contains no original investigations.

‡ Vol. ii. pp. 256—258.

be determined approximately. Physiologists have varied in their estimates, according to the manner in which they tried to determine the point, from 8·5 to 44 pounds. In the present day the blood is generally estimated at about 22 pounds, which is equal to about the eighth part of the weight of the whole body. From experiments on two decapitated criminals (young men) Lehmann believes that this number is too high, and estimates the quantity at about 18 or 19 pounds.

The functions and ultimate disintegration of the blood-cells.

(224.) We pass, without notice, the numerous recent investigations regarding the origin and seat of formation of the blood-corpuscles (both colourless and red) because this is a subject pertaining almost exclusively to histology.* Various functions have been assigned to the blood-cells. Liebig and Mulder, although holding very different views as to the mode in which the process was effected, concurred in the idea that the red corpuscles were conveyers of oxygen to the tissues, and the removers of carbonic acid from them, the oxygen being taken up by them in the lungs when they gave off their carbonic acid. Although Henle and other physiologists have brought forward various observations which seem opposed to this theory, it is so strongly supported by the fact that neither the intercellular fluid nor the serum alone has the power of absorbing more than a very small quantity of oxygen, while the cell-containing blood exhibits a great capacity for absorption, that we may regard the view which ascribes to the corpuscles the function of absorbing oxygen and giving it partially off in the capillaries as completely established. The second part of the theory, viz. that they carry carbonic acid from the tissues to the lungs, is however not so firmly established, for the intercellular fluid exhibits a considerable capacity for dissolving carbonic acid, and hence

* The subject is fully discussed in Lehmann's Physiological Chemistry, vol. ii. pp. 270—274; Kölliker's Manual of Human Histology, translated by Busk and Huxley, vol. ii. pp. 342—347; and Funke's Wagner's Physiologie, p. 132, where the functions of the blood-cells are also very ably considered.

the co-operation of the blood-corpuscles would not be required.

After what has been already stated regarding the action of oxygen on the colour of the blood (see p. 212) and on the hæmatocrystallin (see p. 95), the question becomes almost unnecessary, whether the oxygen is only mechanically taken up by the corpuscles, or whether it enters into chemical combination with some of the constituents of the corpuscles, and thus directly gives rise to the formation of carbonic acid in the capillaries. Both these modes undoubtedly occur. It is clearly proved by numerous experiments that the greater part of the oxygen absorbed in the lungs is only mechanically taken up, or is conveyed to the capillaries in a very unstable form of combination. And direct observations show us that the corpuscles are acted upon chemically by oxygen: the difference in the chemical constitution of arterial and venous corpuscles can scarcely be explained except by the assumption of a chemical action of the oxygen upon the corpuscles or some of their constituents in the lungs. Lehmann found the mineral substances and the hæmatin augmented in the corpuscles after the inspiration of oxygen, whilst the organic substances, and especially the fats, are either destroyed by oxidation and their products of decomposition transferred to the intercellular fluid, or at all events they undergo a considerable diminution of weight by the formation of water and carbonic acid.

The blood-corpuscles must be regarded as cells having special contents, and their activity of metamorphosis must vary with the nature of the fluid in which they are suspended (the plasma). The actual metamorphoses that result from the reciprocal action of the cells and the plasma are not however yet accurately known. "As far as we are at present able to form an opinion on this subject, we think we shall not be deviating very widely from the truth if we regard the blood-cells as organs, that is to say, as laboratories, in which the

individual constituents of the plasma are prepared for the higher function of aiding in the formation and reproduction of the tissues."*

The blood-corpuscles, like all other vital cells, doubtless have a definite period of existence, although we do not know what that period is, and the mode and process of their disintegration are equally unknown to us. We know this much, however, that the cells of the same blood vary in the length of time during which they can resist destructive chemical agents, and hence it is conjectured that the cells which first give way are the old ones. We may presume, from a comparison of the blood taken in repeated venesections, that the life of the red corpuscles is not very short, for the great deficiency of these bodies in the blood for a comparatively long period after repeated or copious venesections proves that their regeneration is not very rapid.

The question whether the blood-corpuscles are generally disintegrated throughout the whole circulating system or at one definite spot, is still undecided. The liver was formerly regarded (by Schultz and F. C. Schmid) as the special seat of this destructive process, but recent comparative analyses (by Lehmann) of portal and hepatic venous blood show that, on the contrary, the liver should rather be regarded as an organ for the regeneration of these cells. The view, supported on histological grounds by Kölliker and Ecker, that the spleen is the principal seat of disintegration of the blood-corpuscles, is strongly confirmed by the investigations of Scherer, to which we have referred in p. 243. He found in the splenic juice various transition stages of the products of decomposition of the albuminous bodies and of the blood-pigment itself, and it seems almost definitely established from his researches, that the spleen aids in the destruction of those corpuscles which are no longer fit for the due performance of their functions.

* Lehmann's Physiological Chemistry, vol. ii. p. 278.

## SECTION II.—THE CHYLE.

The chyle: its physical characters.

(225.) The chyle differs very considerably in its physical characters, according as it is obtained from an animal during digestion or while fasting, and according to the part of the chyliferous system from which it is procured; moreover, the nature of the food very considerably modifies the character of the chyle. For chemical examination it is most conveniently obtained from the thoracic duct, at or near the point where it opens into the subclavian vein. During digestion, especially if fat has been present in the food, it presents an almost milk-white appearance; while in animals that have not recently taken food, it is only opalescent, and varies from a yellowish white to a pale red colour: it has a faint animal odour, a saline and somewhat mawkish taste, and a very slight alkaline reaction. Like the blood, it coagulates in nine or ten minutes after its removal from the body; the coagulum, which usually continues to contract for about three hours, is relatively much smaller than that of the blood, and is very soft and friable, being often a mere jelly. It is usually of a pale yellow tint, but becomes of a pale red colour on exposure to the air. The serum of the chyle always remains somewhat turbid, and it is rendered clearer by ether, which takes up the fat, and generally becomes more opaque on the addition of acetic acid. On boiling it we seldom have a decided, curdy coagulation; but it generally assumes a milk-white appearance from suspended molecules of coagulated albumen.

Its morphotic elements.

(226.) True or typical chyle, that namely which accumulates during the latter stages of digestion, is very rich in morphotic elements; being an extremely plastic fluid, it presents almost every phase of cell-development. We find an abundance of fine molecular granules, spherical aggregations of these granules, cytoid corpuscles, with a simple or divided nucleus (chyle-corpuscles), and fat-globules (see

*Plate V. fig.* 6). It is doubtful whether there is any essential perceptible difference between these chyle-corpuscles, the lymph-corpuscles, and the colourless blood-cells.

Its chemical constituents.

(227.) The chemical constituents of the chyle are fibrin, albumen, fat, salts, and the so-called extractive matters.

The fibrin of the chyle appears to be less perfectly elaborated than that of the blood: it is far less contractile, often remaining in a gelatinous form, and frequently redissolving after its coagulation; under the microscope it does not exhibit the fibrous texture of firmly-coagulated blood-fibrin, and dissolves much more readily than the latter in saline solutions. Its quantity has not been determined in human chyle, but is far less than occurs in the blood.

The albumen is combined with more alkali than in the blood: hence, on boiling the chyle-serum, we do not observe a coagulation in flakes or clots, but the fluid becomes opaque and milky, and a similar effect is produced on the addition of acetic acid. On evaporation it forms a colourless membrane on the surface. The quantity of albumen in the chyle-serum is much smaller than in the serum of the blood.

The presence of casein in the serum of the chyle has been maintained by some chemists, but cannot be regarded as established.

There is usually a considerable quantity of fat in the chyle, some of it being saponified and some existing as free fat. Its amount is very variable, being chiefly dependent on the nature of the food.

With regard to sugar, Lehmann observes that it can only be found in the chyle after the use of amylaceous food, and then only in traces; while Bernard maintains that sugar is present, but that it is conveyed into the chyle by the hepatic absorbents.

The solid residue of the chyle yields about 12% of mineral constituents, of which more than three-fourths are soluble salts. Alkalies abound in this fluid, being partly combined

with albumen, the fatty acids, and lactic acid, and partly with phosphoric acid and chlorine. Of 9·4% of soluble salts, which were yielded by the solid residue of the chyle of a cat, 7·1 parts were chloride of sodium. It is a disputed question whether or not there is any iron in the serum of the chyle, but the probability is that, as in the case of the blood, it can only be regarded as a normal constituent of the corpuscles.

(228.) With regard to the influence of the food on the composition of the chyle, it may be regarded as established, that when an animal is being starved, or kept on insufficient diet, this fluid becomes poorer in solid constituents, and especially in fat, so that it appears merely turbid, and loses its milky colour. This milkiness is due solely to the fat taken in the food, and has no special connection with a purely animal, or purely vegetable diet. Influence of food.

The changes which the chyle undergoes in its course from the intestinal villi to the thoracic duct, are more amenable to microscopical than to chemical investigation. It is in its passage through the mesenteric glands that fibrin first appears in the chyle; and the albumen and solid constituents generally, with the exception of the free fat, are augmented after it reaches the receptaculum chyli; the fat being partly saponified, and partly entering into the formation of the chyle-corpuscles.

Nothing definite is known regarding the morbid conditions of the chyle.

(229.) Various attempts have been made to determine the quantity of chyle poured into the blood; some physiologists * having endeavoured to collect it by opening the thoracic duct in the neck of a living, or just killed animal, and others †, having formed estimates by a comparison between the albu- Quantity of chyle.

* Cruickshank, Magendie, also Bidder (in Müller's Arch. 1845. p. 46).

† Vierordt (in Arch. f. Phys. Heilk. vol. vii. p. 281), and Lehmann (Phys. Chem. vol. ii. p. 291).

minates or fats that are absorbed, and the quantities of those substances found in the chyle. It would appear from the latest investigations on this subject, that the quantity of chyle poured into the subclavian vein in twenty-four hours, is probably about the same as the whole mass of the blood, that is to say, about one-fifth of the weight of the body.

## SECTION III. — THE LYMPH.

Thelymph: its physical properties.

(230.) The lymph is a colourless, or faintly yellowish-red, slightly opalescent fluid, of a rather saltish taste, and with an alkaline reaction. It coagulates in from four to twenty minutes after its removal from the lymphatic system, and then forms a jelly-like, colourless, or pale red coagulum, which continues for some time to contract, so that at last the clot is very small in proportion to the serum.

The lymph that has been submitted to chemical analysis has usually been such as has spontaneously flowed from wounds. It is a matter of great difficulty to find and lay open the lymphatics in the higher animals, and to obtain their contents free from blood and other admixtures.

Its morphotic elements.

(231.) Besides fat globules and nucleus-like formations, we observe on microscopic examination, large numbers of cytoid corpuscles (the lymph-corpuscles), which do not essentially differ from the colourless blood-cells, or from mucus- or pus-corpuscles. Blood-corpuscles have only been found in the lymphatics of the spleen, and in the lymph of starving animals.

Its chemical constituents.

(232.) The chemical constituents of the lymph seem to be precisely those of the blood, if we except the substances peculiar to the red corpuscles; as may be seen by the following analysis made by Scherer*, of fluid obtained from the sac-

* Verhandl. d. phys.-med. Gesellschaft zu Würzburg, vol. vii. p. 268. This is probably the most correct analysis of the lymph that has yet been made.

cular, distended lymphatics of the spermatic cord of a man. The quantity obtained weighed 13·456 grammes, or about 215 grains. The clot weighed 1·005 grammes, or 0·371 $\frac{0}{0}$. In 1000 parts of lymph he found —

| | |
|---|---|
| Water . . . . . | 957·60 |
| Solid constituents . . . . | 42·40 |
| Fibrin and lymph-corpuscles . | 0·37 |
| Albumen and extractive matter . | 34·72 |
| Inorganic matters . . . | 7·31 |

The ash contained a somewhat large amount of chlorine, phosphoric acid, and sulphuric acid, a good deal of potash, some soda, small quantities of earthy phosphates and iron, and no carbonic acid.

From the older analyses referred to in the note, Lehmann infers that the quantity of fibrin in the lymph, as compared with that in the blood-plasma, is very small; that the quantity of albumen is relatively smaller, and that of salts relatively larger; that the lymph contains far less solid constituents than the blood-plasma; that the fat occurs in small quantities, and for the most part in a saponified form; that the extractive matters occur in larger quantity in the lymph than in the blood-serum; and that salts of ammonia and pre-formed sulphates, are found in considerable quantities.

Its quantity.

(233.) From Bidder's experiments on animals, he infers that thirteen kilogrammes, or upwards of 28lbs. of fluid, pass through the thoracic duct of an adult man into the subclavian vein in the course of twenty-four hours. If his view be correct, that not more than about three kilogrammes of true chyle (the product of digested food) are formed daily, the remaining ten kilogrammes, or 22lbs., must represent the quantity of true lymph formed in twenty-four hours.*

Other analyses by Gmelin, Marchand and Colberg, L'Heretier, Dr. Rees, Lassaigne, and Nasse are given in my translation of Simon's "Animal Chemistry," vol. i. pp. 351—353.

* See, however, the statement, regarding the daily quantity of chyle, in last page.

## SECTION IV. — TRANSUDATIONS.

Transudations distinguished from secretions and exudations.

(234.) Under the term, *transudations*, Lehmann, and other recent writers on Physiological Chemistry, include those fluids which consist of liquid constituents of the intercellular portion (or plasma) of the blood which have transuded in an unchanged state through the capillaries. They are distinguished from *secretions*, in the strict sense of the word, by their containing neither any peculiar element, nor any accumulation of matters that exist only sparingly in the blood; and from *exudations*, on various grounds, which will be noticed when we speak of the latter class of fluids, and of which it is sufficient to mention one in the present place, namely, that the latter are due to morbid action, while the former depend on purely physical laws. Hence, we include among the transudations, the normal secretions of the various serous membranes, the tears, the aqueous humour of the eye, the liquor amnii, and the parenchymatous fluid which moistens and nourishes the tissues.

Conditions on which transudation is dependent.

(235.) The escape of the water and of the other constituents of the plasma through the walls of the capillaries, is solely dependent on physical conditions; namely, on the penetrability of the walls of the capillaries, on the rapidity of the motion of the blood within them, and on the physical and chemical characters of the circulating fluid. As these conditions vary, so will the transudation be more or less modified in its physical or chemical characters. But all transudations (whether normal or excessive) have in general much the same properties as the intercellular fluid itself; they are colourless, transparent, of a faintly saline taste, and of an alkaline reaction; and their specific gravity is usually somewhat lower than that of the intercellular fluid, or of the serum of the blood.

(236.) The morphotic elements which they contain are dependent on the surfaces on which they are effused; and hence we may meet with epithelial structures, molecular granules, cytoid corpuscles, &c. Red corpuscles can only occur when there has been laceration of the capillaries, and their presence indicates that we are not dealing with a pure transudation. Morphotic elements.

(237.) Transudations are never thoroughly identical in their chemical composition with the intercellular fluid of the blood; for the different constituents permeate the walls of the capillaries with different degress of facility; and as water permeates most readily, it necessarily follows that transudations must contain a larger amount of this constituent than the plasma. Again, since the soluble salts and the extractive matters permeate animal membranes more readily than albumen, and since albumen permeates them more freely than fibrin, we find that the transudations, as contrasted with the plasma, contain a relative excess of salts and extractive matters, and a relative deficiency of albumen; while fibrin is either present in extremely small quantities, or is altogether absent. Chemical characters.

(238.) No fibrin is usually found in normal transudations from serous membranes, or in those effusions which occur without an inflammatory condition of the capillaries; hence it is absent in those cases of accumulation of fluid, which arise from a disturbance of the function of the lymphatics, or from an excess of water in the blood. If, however, the blood-current be much impeded, or if it be perfectly stopped in the capillaries, fibrin always escapes through the attenuated walls of the vessels. Some capillaries may, in their normal state, allow the transmission of fibrin, a view that is supported by the occurrence of fibrin in the lymph, and by its constant presence in the ordinary plastic exudations; as for instance, in the non-sanguineous secretion of fresh incised wounds. Fibrin.

Fibrin may often be contained in transudations, when from

its small quantity, and from its having already undergone some change, it may escape detection. Even assuming (which is not the case) that fibrin passed into transudations with the same facility as albumen, and recollecting that in the plasma the fibrin does not amount to more than one-twentieth of the albumen (4·05 : 78·84, see pp. 205—207,) it is obvious that transudations could never contain more than very minute quantities of fibrin; and if we further consider that the fibrin in the parenchymatous juices is very rapidly applied to the reparation of tissues, and in morbid transudations to the formation of false membranes, &c., we need not wonder that it is so often absent.

No fibrin can be detected in those normal transudations which occur in the animal body; as, for instance, in the moisture of serous sacs, the aqueous humour of the eye, the tears, the liquor amnii, certain dropsical effusions, in cutaneous vesicles or bullæ (whether artificially excited or consequent on a skin disease), or in secretions from the intestinal capillaries, as in the diarrhœa arising from intestinal catarrh or drastic purgatives, or accompanying cholera.*

In those inflammatory conditions in which fibrin is found in the transudations, its quantity may be very variable, but will always be less (in the case of recent effusions) than that existing in the corresponding plasma. The fibrin in these fluids usually forms a loose gelatinous coagulum, but in all other respects seem to be identical with blood-fibrin.

Albumen. (239.) The albumen occurring in transudations in no way differs, either chemically or physically, from the albumen of the blood. It frequently happens, however, that the whole, or part of the albumen in transudations assumes a casein-like

* In opposition to the statement contained in the text, it should, however, be observed that Tilanus (De Saliva et Muco, Amstelodami, 1849, p. 72) found true coagula in the fluid contained in a blister caused by boiling water; and that Picard (De la Présence de l'Urée dans le Sang, Strasbourg, 1856, p. 34) saw the contents of an ordinary blister coagulate like frog's blood from which the cells had been removed.

character; that is to say, it does not coagulate on heating, is precipitated by dilute acetic acid, and separates in the form of a superficial membrane on evaporation; these are, as we have seen in p. 106, the characters of albuminate of soda, which is more abundant in these transudations than in the blood.

The quantity of albumen in different transudations is very variable. It is scarcely to be detected in the tears, in the aqueous humour of the eye, in the liquor amnii (in the latter stages of pregnancy), in the fluid of the lateral ventricles and of the spinal canal, and in the fluid of the connective tissue in œdema of the extremities; while in the fluid of hydrocele Lehmann found as much as 6·283%, and in a peritoneal effusion Hoppe found 7·73% of albumen. This variation is, however, by no means arbitrary, but is dependent on certain propositions or conditions, for the knowledge of which we are chiefly indebted to C. Schmidt.

The following are the most important of these propositions: —

*a. The quantity of albumen seems to be dependent on the system of capillaries through which the transudation has been effused.*

Schmidt arrived at his knowledge of this proposition by a series of carefully conducted parallel analyses of normal and abnormal transudations. He found the transudation in the pleura to be richest in albumen (2·85%), that in the peritoneum considerably poorer (1·13%), that within the cranial membranes yet more deficient in this substance (0·6 to 0·8%), and that in the subcutaneous connective tissue the poorest (0·36%). He found the albumen in these proportions in the transudations of the same person, who died with Bright's disease; and he convinced himself, by further investigations regarding the normal transudation of the cerebral capillaries and hydrocephalic effusions, that not only does the relative quantity of albumen always remain tolerably equal when there is an excess of the transudation, but also when, after

the removal of the old effusion, a new transudation occurs through the same capillaries.

His observations in support of this proposition are confirmed by corresponding analyses by Lehmann and other chemists*; but, like most natural laws, this law is so modified in its results by other laws, that its direct recognition is not very obvious. It is not true that under *all and the most varied conditions* the quantity of albumen in the transudation yielded by the same group of capillaries is always in precisely the same ratio. The proposition is only true to this extent, that when, under equal conditions, there are several excessive transudations effused from various serous membranes, we have one and the same proportion between the quantities of albumen in the transudations of the different sets of capillaries. Although the transudation is doubtless very much influenced by the thickness or the delicacy of the capillaries, its composition, and consequently its amount of albumen, will vary with other conditions which we shall now proceed to notice.

*β.* Another proposition deducible from the analyses of Schmidt, Lehmann, &c., is, that *the amount of albumen in the transudation is proportional to the slowness with which the blood permeates the capillaries.* Thus, for instance, in transudations into the peritoneal cavity, we find more albumen when they are caused by the pressure of large tumours on the abdominal veins, than when produced by lesser mechanical obstructions, such, for instance, as incipient cirrhosis; and similarly, the albumen is more abundant in the effusion in acute than in chronic hydrocephalus.

*γ.* Finally, *the amount of albumen in a transudation is always dependent on the quantity of albumen in the blood.* Thus, for instance, in Bright's disease, where the kidneys are

* A detailed account of these analyses is given in Lehmann's Physiological Chemistry (English edition), vol. ii. pp. 316—318; and in Lehmann and Huppert's Zoochemie, 1858, pp. 236–238.

continuously removing albumen from the blood, the transudations are very poor in albumen; and all dropsical effusions which originate in disturbances in the circulating system, are richer in albumen than those which depend upon too watery a state of the blood.

(240.) The other constituents of transudations require a comparatively brief notice.

Casein.

True *casein* has never been found in these fluids.

Extractive matters.

The *extractive matters* always occur in larger quantities in the transudations than in the serum of the corresponding blood; and they are more abundant in the older stagnating fluids than in those that have been more recently separated, and in serous than in fibrinous transudations; thus, whilst in the serum of normal blood the albumen is to the extractive matters as 100 to 5, it is as 100 to 8, or even to 16, in fresh fibrinous transudations; and in fresh serous transudations it is as 100 to 12, or even to 30; and in older ones as 100 to 42, or even to 86. Hence, it might be inferred that these substances transude through the capillaries in larger quantities than the albumen; and this is proved to be the case by the analyses of normal transudations; as, for instance, the fluid within the pericardium, the cerebral and spinal fluids, the liquor amnii, the tears, and the aqueous humour, in which the ratio rises to 100 : 300; indeed, the quantity of albumen may be so diminished as to be scarcely quantitatively determinable. The amount of extractive matters seems generally to vary with the composition of the blood, and with the group of capillaries through which the fluid has been effused. It must further be recollected that in the transition of albumen into textural elements, which occurs during the organisation of a transudation, a portion of the albumen yields extractive matters, which thus in part accounts for the absolute and relative augmentation of the last-named substances.

We find a smaller proportion of *saponifiable* and *saponified fats* in transudations than in the corresponding plasma

of the blood; but in these cases also the capillaries seem to exert a certain influence, for the fluids exuded by the capillaries of the arachnoid membrane, the pericardium, and the subcutaneous connective tissue, are especially poor in fatty matters.

*Cholesterin* usually occurs in larger quantities in these fluids than the fats and fatty salts; indeed, in some cases (in the fluid in ovarian dropsy and in hydrocele) it occurs in such quantity that these transudations present the appearance of opaque fluids, or even of semi-fluid masses.*

*Bile-pigment* has not only been observed in the transudations in cases of jaundice, but also in normal transudations. Lehmann found it in considerable quantity in two cases of hydrocele.

Sugar.

*Sugar* has been found in the serous fluids in diabetes, even in the serum obtained from the application of a blister. It is generally believed that no sugar occurs in the pleuritic, peritoneal, and pericardial transudations of non-diabetic patients; but Grohé† found sugar in the transudations in a case of chronic pleurisy and in a case of epilepsy; and Frerichs found it in the fluid of ascites in the case of a girl, aged nine years, suffering from fatty liver. Lehmann, on the other hand, sought in vain for it in more than three pints of a peritoneal transudation obtained from a drunkard with granular liver. Bernard maintains that the peritoneal transudations of rabbits and horses, especially when they have been fasting for some time, contain sugar, which takes its origin from the lymphatics of the liver. Sugar, or at all events a substance which reduces oxide of copper (Trommer's test), occurs in the cerebro-spinal fluid and in the liquor amnii.

* In a hydrocele-fluid, which formed a tolerably consistent pulp, Lehmann found 3·041% of pure cholesterin, amounting to 38·2% of the solid residue. This substance likewise occurs abundantly in the fluid of the choroid plexus, and in transudations into the peritoneum and pleura.

† Verhandl. d. phys.-med. Gesellschaft zu Würzburg, vol. iv. p. 2.

We have already (see p. 46) noticed the presence of *urea* in the fluids of the eye * and in the liquor amnii. It has been found by Schmidt in the fluid of chronic hydrocephalus; by Grohé and others in pleuritic and pericardial effusions, even when there was no apparent disease of the kidneys; by Picard, in the fluid obtained from the application of a blister in a case of ascites; by F. Müller, in the fluid of hydrocele; by Redenbacher †, in the peritoneal effusion in cirrhosis of the liver; and by Wolff, in the fluid of ranula. In Bright's disease it occurs in all the fluid effusions.

Since urea is often found in considerable quantity in the transudations, we might naturally expect to find some of the other products of regressive metamorphosis, such as uric and hippuric acids, creatine, creatinine, &c. Hitherto, however, none of these substances have been detected, excepting *creatinine*, which Scherer thinks that he has found in the liquor amnii.

Organic acids.

In some of those cases of puerperal fever in which the blood assumes an acid reaction, Scherer has found *lactic acid*

* In the fluids of the eyes of a woman, who died from puerperal peritonitis and pleuritis, Picard found 0·5% of urea.

† Redenbacher in an inaugural dissertation, Ueber die Zusammensetzung hydropischer Transudate bei Lebercirrhose, 1858, gives two analyses of such transudations, both of which contained urea. The composition of these fluids which were obtained by paracentesis was as follows :—

In 1000 parts there were contained—

| | (1.) | (2.) |
|---|---|---|
| Water | 947·1713 | 986·666 |
| Albumen | 42·0500 | 8·490 |
| Urea | 1·1214 | 0·776 |
| Chloride of sodium | 2·5233 | 0·874 |
| Fatty and extractive matters | 3·0240 | 1·461 |
| Fixed salts | 4·1100 | 1·733 |
| Sulphuric and phosphoric acids | traces | traces. |

The whole quantity of the discharged fluid in the first analysis weighed 12,380 grammes, or between 24 and 25 lbs.; its specific gravity was 1·018, and it contained 13·9 grammes, or about 214 grains of urea; while the fluid which yielded the second analysis amounted to 18,900 grammes, or 37 lbs., had a specific gravity of 1·008, and contained 14·7 grammes, or 226 grains, of urea.

in the transudations, in one case as much as 0·105% of the free hydrated acid. Lehmann believes (although he has not definitely proved) that lactates frequently occur in transudations. *Succinic acid* has been found (see p. 16) in the fluid contents of hepatic cysts containing echinococci, and in the fluid of hydrocele; and *acetic acid* was once discovered by Simon in the fluid of pemphigus. Generally, however, the fluids in pemphigus, herpes, and eczema, are alkaline, and contain albumen.

The *soluble salts* transude in a comparatively greater ratio than the organic substances, and always occur in the effused fluids in nearly the same proportion as in the corresponding blood-serum. In dropsy complicated with Bright's disease, we frequently, however, have an exception to this rule, for the salts in the transudations then often exceed those of the blood-serum.

No *salts of ammonia* can be detected in normal and recent transudations.

Like all the animal fluids, the transudations contain *gases;* of these carbonic acid is most abundant, but oxygen and nitrogen also admit of being determined with certainty.

# CHAPTER XII.

## THE FLUIDS CONNECTED WITH GENERATION AND DEVELOPMENT.

### SECTION I.—THE SEMINAL FLUID.

(241.) The seminal fluid, as it occurs after ejaculation, is mixed with the secretion of the prostate and other smaller glands. In this state it is a viscid, opalescent, colourless substance (which however becomes yellowish on drying) with a peculiar odour; it is considerably heavier than water, and neutral or faintly alkaline; when freshly discharged it is somewhat gelatinous, but after standing for some time it becomes thoroughly fluid, and, if mixed with water, forms a mucous sediment; it is coagulated by the action of alcohol, but not by that of heat. Its general character.

In order to procure the seminal fluid in a state of purity we must obtain it from the *vasa deferentia* or the *vesiculæ seminales* of animals in the rutting season; but in this way we cannot obtain it sufficiently copious for chemical analysis. It has sometimes been obtained for chemical examination (in the case of fishes) by incising and pressing the testicles.

The characteristic morphotic elements of the semen are the seminal filaments or spermatozoa. As their form and measurements are given in all recent works on physiology, it is not necessary for us here to do more than mention what little is known of their chemical constitution, and of the effect of various chemical reactions on them. It appears from the researches of Frerichs that the spermatozoa obtained from the Its morphotic elements.

carp (and the semen of fishes, birds, and mammals possesses, according to him, essentially the same chemical composition) "consist of binoxide of protein, the same substance which Mulder has proved to be the principal constituent of the epithelia, as well as of the horny tissues in general, and contain about 4% of a butter-like fat, as well as phosphorus in an unoxidised state and about 5% of phosphate of lime."*

Kölliker has recently studied the effects of various reagents on the vitality of the spermatozoa. The following are some of the most important of his results. (1.) Water, and watery solutions of innocuous neutral substances and salts, suspend the motions of the spermatozoa. (2.) In the solutions of many indifferent organic substances of moderate concentration (of the various kinds of sugar, of albumen, urea, glycerin, salicin, and amygdalin) the spermatozoa seem unaffected. (3.) Some solutions of indifferent organic substances, even in a state of concentration, act like water, as for instance gum arabic, vegetable mucilage, and dextrine. (4.) Many organic substances suspend the motions of the spermatozoa by exerting a chemical action on them, as for instance, alcohol, creosote, tannin, and ether, while other substances, as most of the oils mechanically produce the same effect. (5.) Metallic salts, even when extraordinarily diluted (as for instance one part of corrosive sublimate in 10,000 parts of water), destroy their motions. (6.) Solutions of most of the alkaline and earthy salts exert a deleterious influence, destroying them in from 1 to 4 hours. (7.) Acids, even when very diluted (as for instance one part of hydrochloric acid in 7500 of water), soon prove fatal.

Its chemical composition.

Our knowledge of the chemical composition of the seminal fluid is not satisfactory. Vauquelin found in ejaculated human semen 6% of organic matter, to which he applied the name of *spermatin;* Kölliker found in the seminal fluid of a

* Cyclopædia of Anatomy and Physiology. Art. Semen, vol. iv. p. 506.

bull 15·265% and in that of a horse 16·449%. The fatty matter in the bull's semen amounted to 2·165%. The same salts occur in the semen as are found in the blood, phosphate of lime and especially phosphate of magnesia preponderating. In the fluid filtered portion of the seminal fluid of the carp Frerichs found an excess of chloride of sodium together with alkaline phosphates and sulphates.

## SECTION II. — THE FLUIDS OF THE EGG.

(242.) The egg in its fresh state consists mainly of the *yelk*, which in the case of birds is surrounded by a tolerably thick layer of *white*, or albumen, and is invested by a calcareous envelope, the shell.

The yelk; its morphotic elements and chemical composition.

We know little regarding the chemistry of the yelk except in the case of birds and fishes.* It occurs as a viscid, thick, yellowish red, or purely yellow inodorous fluid, with a slight but a peculiar taste; mixed with water it forms a white emulsion; it has a slightly alkaline reaction, solidifies on boiling, coagulates in cold alcohol, and when shaken with ether yields to that fluid a reddish or amber-coloured fat, while a tough white mass is precipitated.

On examining the yelk under the microscope we find that it consists of yelk-corpuscles and fat-globules of various sizes interspersed between immeasurably minute granules. The fat-globules are distinguished by a less intense yellow colour, and by being covered with a layer of fine granules. while the yelk-corpuscles are invested with a capsule which is usually dotted with granules.

* It is true that Valenciennes and Frémy (Journal de Chim. et de Pharm. 3 sér. 1854, vol. xxvi. pp. 5—16, 321—326, and 415—423; and Sillimann's Journal, 1855, vol. xix. pp. 38—48, 238—243, and vol. xx. pp. 65—72) have examined the yelk in birds, fishes, amphibia, crustacea, insects, and mollusca; but they describe so many new, and probably doubtful, proximate principles (ichthin, ichthulin, ichthidin, and emydin), that I have not deemed it expedient to introduce their investigations into the text.

The yelk-corpuscles consist chiefly of fat containing phosphorus (probably glycero-phosphoric acid) and of the yelk-pigment; and the capsules amount to about 0·5% of the yelk.

The molecular granules interspersed through the yelk consist of casein which dissolves readily in alkaline salts; this casein forms about 14% of the yelk.

Albumen. Albumen is likewise a constituent of the yelk; it occurs in a dissolved form and amounts to about 3%.

Vitellin. The substance formerly known as vitellin and described as a constituent of the yelk, is merely an admixture of casein and albumen (see p. 114).

Fat. The fats occurring in the yelk have not yet been thoroughly examined. They consist, however, principally of margarin and olein in association with a substance which, in its high point of fusion and its crystalline form (rhombic tablets), closely resembles cholesterin, with which however it is not perfectly identical. Lecithin and cerebrin (two substances discovered by Gobley in the substance of the brain and which will be noticed in the section "On the Brain and Nervous Tissue") are said also to occur in the yelk-fat. The latter probably gives origin to the glycero-phosphoric acid which has been detected in the yelk. The collective fats amount to about 30% of the yelk-fluid.

Sugar. Lehmann invariably found grape-sugar in the yelk.

Pigments. The pigments have not been thoroughly examined. We know little more than that there is both a yellow and a red pigment and that at least one of them contains iron.

Potassium compounds and phosphates. In examining the mineral constituents of the yelk we find a great preponderance of the potassium-compounds and the phosphates; chlorine and sodium being present in extremely minute quantities. The ash contains from 67 to 70% of phosphoric acid, and consequently the phosphates must be monobasic. The total amount of mineral constituents averages 15% of the yelk.

The water in the yelk varies considerably, ranging from 48 to 55%. Water in yelk.

The egg of the common hen contains on an average 15·2 grammes (234 grains) of yelk and 23·9 grammes (368 grains) of white.

The most important constituent of the white is albumen, which is for the most part in combination with soda; it amounts to about 12·5% of the whole white. The white of egg.

Margarin occurring in heaps of acicular crystals may be detected by the microscope in the white, which also contains olein, and oleate and margarate of soda.

Grape-sugar occurs in the whites both of fresh and of incubated eggs, and averages 5% of the dried residue. Sugar.

The mineral constituents of the white consist chiefly of soluble salts — the reverse of what occurs in the yelk. The ash contains about 50% of chlorides, while the phosphates and potassium-compounds occur in comparatively small quantity. Some of the soda is combined with carbonic acid. A little silica occurs both in the white and in the yelk, and fluorine has been detected in the former. The fresh white contains on an average 0·66% of mineral constituents. Salts.

The water contained in the white ranges from 82 to 88%. Water.

The shell of the egg, both in birds and amphibia, consists almost entirely of carbonate of lime (about 97%), with a little phosphate of lime, traces of magnesia, and a very little organic matter.

The variety of colour on the eggs of different birds seems to be due to certain modifications of the bile-pigment with which the egg comes in contact in the cloaca. (Wicke.)

We know little or nothing regarding the chemical changes which the egg undergoes during incubation.

(243.) After nine days' incubation, the amnotic fluid is found to be of a pale yellow colour, and to contain little albumen; after fourteen days' incubation, it contains so much albumen that it solidifies on heating. Its reaction is alkaline. The amnotic and allantoic fluids of the chick.

The allantoic fluid is, at the commencement of incubation, very limpid, and contains no albumen; after fourteen days incubation it has become turbid, from the separation of uric acid; and after seventeen days, it is found to have become opaque, of a yellowish-white colour, and faintly acid in its reaction. It deposits uric acid freely, and is said to contain urea.

The fluids of the mammalian ovum.

For the following facts regarding the mammalian ovum, we are mainly indebted to the researches of Schlossberger * and Majewski.†

The liquor amnii.

The liquor amnii in the embryo of the sheep and the pig is always clear and colourless; in that of the cow it is clear and colourless at a very early period, but subsequently becomes yellow, viscid, and turbid; it is always alkaline in its reaction. It is always poor in solid constituents, which, however, increase during the process of fœtal development from 0·55 to 1·9%. Albumen is always present, in proportions ranging from 0·1 to 0·2%, but diminishes, and sometimes quite disappears towards the end of fœtal life (at all events in the human subject), and is replaced by a mucin-like substance, which occurs in considerable quantity. Neither true casein nor fibrin exists in it. Sugar is found in considerable quantity (from 0·06 to 0·19% in the sheep, and from 0·1 to 0·3% in the cow) in the liquor amnii of herbivorous animals; it occurs in mere traces in this fluid in the pig, and is altogether absent in man. (This observation is in complete accordance with Bernard's ‡ recent discovery of special glycogenic cells in the placenta in some animals (rodents) and in the amnion of others.) Urea is always present and increases with the age of the fœtus, its maximum quantity being about 0·4%. The mineral substances consist chiefly of phosphates

* Ann. d. Ch. u. Pharm. vol. xcvi. pp. 67—75, and vol. ciii. pp. 193—199.

† De Substantiâ, &c. Diss. Inaug. Dorpat, 1858. I have not had an opportunity of seeing this thesis. The results are quoted by Lehmann.

‡ Compt. Rend. vol. xlviii. pp. 77—86.

and of chloride of sodium, and, like the urea, increase with the age of the fœtus; they range from 0·14 to 0·75%. In the liquor amnii of the cow the mineral are to the organic matters in about the ratio of 1 to 1·5.

The allantoic fluid more closely resembles the amniotic in its chemical characters than we should have expected from their different physiological relations. At an early stage it is colourless, but subsequently becomes yellow or reddish. Its reaction is always alkaline. Its solid constituents increase with the development of the fœtus from 0·65 to 3·83%. It contains no albumen, but urea and sugar are two or three times as abundant in it as in the amniotic fluid. The amount in which its characteristic ingredient, allantoine (see p. 49) occurs in it, has never been definitely determined. The mineral substances are more abundant than in the corresponding liquor amnii, amounting towards the end of pregnancy to 0·876% in the sheep, and 1·073% in the cow.

(244.) The (so-called) uterine milk of the ruminants (the secretion of certain glands lying in the interior of the uterus of these animals) has been examined by Schlossberger. It consists of a cream-like fluid, containing neither casein, fibrin, nor sugar. It has a weak acid reaction, and was found to contain 9·5% of albumen (including cellular structures and extractive matter), 1·5% of fat, and 0·7% of mineral matters, consisting of acid phosphate of alkali and lime, and a little chloride of sodium and iron.

## SECTION III. — THE MILK.

Its physical properties.

(245.) The milk is an opaque white fluid, with frequently a bluish-white or yellowish tinge; it is devoid of odour (except for a short time after its extraction), is of a slightly sweet taste, most commonly of an alkaline reaction, and its specific gravity varies from 1·018 to 1·045, the average in women being 1·032.

When milk has been allowed to stand for some time, a thick, fatty, yellowish-white stratum (the cream) forms upon its surface, while the fluid below has become poorer in fat, of greater specific gravity, and of a more bluish-white colour. Milk does not coagulate on boiling, but a membrane or film of coagulated casein, containing fat-corpuscles, forms upon its surface. If milk be allowed to stand for some time, exposed to air of the ordinary temperature, it gradually begins to exhibit an acid reaction (from the formation of lactic acid from the milk-sugar), and the casein becoming coagulated, the fluid gradually assumes the form of a thickish pulp. Rennet (the dried mucous membrane of the fourth stomach of the calf) rapidly induces coagulation, whether the milk be acid or alkaline.

Its reaction.

Human milk almost invariably presents an alkaline reaction *, that of the carnivora is acid†, while that of the herbivora is generally but not invariably alkaline. In stall-feed animals (cows, mares, and ewes) kept on green food it is however frequently acid.‡

Its morphotic elements.

When examined under the microscope the milk appears as a clear fluid containing fat-globules (the milk-globules) in suspension (see *Pl. V. fig.* 7, *a*). They commonly vary from ·0012 to ·0018‴ in diameter, although a few may usually be seen both above and below these measurements. When simply observed under the microscope, they do not present any evidence of an investing membrane. The existence of such a membrane may however be demonstrated in either of the following ways. First, if we add dilute acetic acid to

* Elsässer (at Schlossberger's suggestion), examined the reaction of the milk in 385 women, most of whom were healthy. In forty-five instances it was neutral, and in all the rest alkaline, and even in these forty-five cases the milk was found on other occasions to be alkaline. Rattenmann obtained a very similar result from an examination of 272 cases.

† Proved by the researches of Bensch (Ann. d. Ch. u. Pharm. vol. lxi. pp. 222—227), Rüff (ibid. vol. lxxxvii. pp. 317—324), and others.

‡ Rüff (Op. cit.) and others.

milk under the microscope, the globules exhibit changes of form which they could not possibly experience if they were mere fat-globules, for they become much distorted and wrinkled, and from most of them small fat-globules are seen to escape. Secondly, if milk be shaken with ether it does not lose its emulsive appearance; but if a little caustic potash be first added, which dissolves the investing membrane, the milk, if it is then shaken with ether (which takes up all the fat) becomes transparent and almost limpid.

The colostrum-corpuscles which occur in the milk for the first three or four days after delivery, and which often present themselves at a later stage if any disease supervenes, are irregular conglomerations of very small fat-globules, which are held together by an amorphous granular matter of an albuminous nature. See *Pl. V. fig. 7, b.*

Epithelial cells, mucous corpuscles, coagula of fibrin, blood-corpuscles, and some of the very lowest forms of vegetation are occasionally found in morbid states, but are not entitled to rank among the normal microscopic constituents of milk.

Chemical constituents.

(246.) The chemical constituents of the milk are casein, fatty matter, sugar, and salts.

Casein.

The amount of casein in human milk has been variously estimated, the differences being probably in a great measure due to the different modes of analysis. The most trustworthy of these estimates are given in the foot-note.* In healthy human milk it seems to range from 2·7 to 3·5%, while in the colostrum (according to Simon) it amounts to 4%. In the milk of the ass it is less than 2%, in that of the cow it

* Clemm determined the quantity of casein at 3·37%, Simon (taking the mean of a large number of cases) at 3·5%, and Haidlen at 3·1%, in good milk, and at 2·7% in an inferior specimen. Vernois and Becquerel, taking the average of eighty-nine cases, found the casein and extractive matters (which they did not separate from each other), to amount to 3·924%, the extremes being 1·932% and 7·092%.

ranges from 3 to 4% , and in that of the bitch from 8·3 to 13·6%.

The quantity of casein increases with the free use of animal food, and diminishes on a vegetable diet.

During the first two months after delivery there is an excess of casein; from the tenth to the twenty-fourth month there is a diminution. (Vernois and Becquerel.)

Fatty matter.

The fatty matters have hitherto been only examined in cows' milk. They collectively form an almost colourless or slightly yellow mass, which after being fused solidifies at about 80° F.; and consists of 68% of margarin *, 30% of olein, and 2% of an admixture of fats, which on saponification yield butyric, caproic, caprylic, and capric acids (or sometimes vaccinic acid instead of butyric and caproic acids).

In woman's milk the fatty matters vary † from 2·5 to 4·3%, in cows' milk they average 4·5%, in mares' milk 6·95%, in asses' milk 1·25%, in ewes' and goats' milk 4%, and in bitches' milk 11%. Human colostrum contains 5%, that of the cow 2·6% and that of the ass 5% of fatty matters.

According to Simon, the quantity of fat contained in woman's milk remains nearly the same throughout the whole period of lactation.

The experiments of Boussingault and others show that in the case of the cow the nature of the food in some degree influences the amount of fat contained in the milk; and Dumas found that the milk of bitches was somewhat richer in fat when they had been fed on vegetable than when they had been fed on animal food.

* The investigations of Heintz tend to show that the solid fat, which we have here designated as margarin, consists of four different neutral fats, which on saponification yield four solid fatty acids, differing from each other by $C_4H_4$, namely, myristic acid $C_{28}H_{28}O_4$, palmitic acid $C_{32}H_{32}O_4$, stearic acid, $C_{36}H_{36}O_4$, and butic acid $C_{40}H_{40}O_4$. (See p. 6.)

† Simon found from 2·53 to 3·88%; Clemm found 4·3% on the fourth day, 3·53% on the ninth day, and 3·35% on the twelfth day; while Vernois and Becquerel found an average of 2·67%, the extremes being 0·666 and 5·642%.

It has been proved by Peligot and Reiset that the milk which is last yielded is much richer in fat than that which is first drawn, although the composition of both portions is otherwise the same. This is true not merely in the cow and the ass, but in respect to woman's milk.

Milk-sugar or lactine varies in human milk from 3·2 to 6·2%, and in cows' milk from 3·4 to 4·3%; in asses' milk it averages 4·5%, in mares' milk 8·7%, in that of sheep and goats 4·3%; the milk of bitches when fed on a purely animal diet often contains mere traces of sugar.

Human colostrum contains about 7% of sugar; the milk six days after delivery contains 6·24%, and the quantity of sugar subsequently diminishes. (Simon.)

The nature of the food exerts a certain influence on the amount of sugar. When fed upon a purely animal diet bitches yield milk containing little or no sugar, but if they are fed on vegetable food their milk contains a considerable quantity of that constituent. (Bensch and Poggiale.)

In the human subject no essential influence seems to be exerted upon the quantity of sugar either by deficient or superabundant food. (Simon, Vernois and Becquerel.)

Milk which is secreted freely and abundantly contains more sugar than milk secreted sparingly. (Vernois and Becquerel.)

Salts.

The salts consist of the chlorides of potassium and sodium and of the alkaline and earthy phosphates, together with potash and soda in combination with the casein of the milk. No sulphates or salts of ammonia are found in fresh milk. A little peroxide of iron occurs in the ash, which likewise contains traces of fluorine. (Wilson.)

The milk of women contains from 0·16 to 0·25% of salts *, cows' milk from 0·55 to 0·85%, and the milk of bitches from 1·2 to 1·5%. The amount of the soluble salts is in general

* Vernois and Becquerel place the salts as low as 0·138%, the extremes being 0·055 and 0·338%.

smaller than that of the insoluble phosphates, in the ratio of 1 to 2 or 3.

Extractive matters.

The extractive matters occurring in the milk have not yet been carefully examined, and little is known regarding either their quantity or their composition.

Gases.

Free gases, and especially carbonic acid, can always be shown to be present in fresh milk.

Lactic acid.

Lactic acid is not contained in the fresh healthy milk either of women or of herbivorous animals. In the occasional cases in which cows' milk has been found acid (see p. 274), it has not been determined whether the acidity was due to lactic acid, to butyric acid, or to the presence of acid phosphates. The milk of the bitch (and probably of all carnivora) is neutral when the animal is kept on vegetable food, while it is always acid when the food has been exclusively animal; in this case the acid reaction is most probably due to superphosphate of lime.

Abnormal constituents.

(247.) Abnormal constituents have seldom been detected in the milk, although daily experience shows us that certain kinds or modifications of milk exert a deleterious effect on the infant.

Albumen.

Albumen, according to Lehmann, is only to be found in the milk in inflammatory affections of the mammary glands, unless, indeed, we regard the coagulable ingredient of the colostrum to be albumen, which is not the case. Other chemists, however (amongst whom we must place Quevenne, Mitscherlich, Doyère, Girardin, Morin, and Bouchardat), maintain that albumen, or a substance closely allied to it, exists as a normal constituent of milk; and Lieberkühn admits that milk, in addition to casein, contains a nitrogenous substance coagulable by heat, which, however, is not (in his opinion) pure albumen, although allied to it. Some protein-substance differing from ordinary casein certainly occurs occasionally in some kinds of apparently healthy milk; for Scherer has obtained a caséin from normal milk which coagulated by

heat; and both Dumas and Bensch found that the milk of the bitch became pulpy, and was even almost coagulated on being heated, when the animal had been kept on vegetable food, as well as when it was fed on animal matters, while on cooling it very frequently again became thinly fluid.

Fibrin and hæmatin may be detected if blood is present. Fibrin.

Urea has been found in the milk in cases of Bright's disease. Urea.

(248.) Much has been written regarding the passage of foreign substances, such as pigments, medicines, and poisons, into the milk. That iodide of potassium enters the milk is unquestionable; Personne has obtained a deposit of mercury on a gold plate from the milk of a woman who had been taking small doses of protiodide of mercury for a fortnight; and Landerer has detected quinine in the milk of a wet-nurse: other chemists have however been less successful. Passage of matters into the milk.

Grape-sugar and cane-sugar do not pass in their unchanged state into the milk; they are converted in the mammary glands into milk-sugar.

(249.) We shall now briefly notice certain physiological conditions of the milk, beginning with the colostrum.

The colostrum generally appears as a turbid yellowish fluid, resembling soap and water, having a viscid consistence and a strongly alkaline reaction. It passes more readily into lactic fermentation than ordinary milk, and exhibits an excess of solid constituents both in women and animals, the augmentation being most marked in cows, asses, and goats, in the casein, and in women in the sugar. The colostrum is richer in fat than the corresponding milk, and contains from two to three times more salts. The colostrum.

(250.) The following physiological influences have been carefully studied by Vernois and Becquerel: — Various physiological influences.

1. The influence of the age of the nurse.
2. The influence of the age of the milk.
3. The influence of the presence of colostrum.

4. The influence of the constitution of the nurse.

5. The influence of the number of children.

6. The influence of pregnancy.

7. The influence of the development of the breast.

8. The influence of the retention of the milk in the breasts.

9. The influence of menstruation.

10. The influence of the colour of the hair.

11. The influence of the food.

12. The connexion between the state of the health of the infant and the milk.

13. The influence of the quantity of the milk.

In order to afford *data* for comparison, we must give Vernois and Becquerel's table of the composition of healthy human milk. This table represents the mean of eighty-nine analyses.

| | |
|---|---|
| Specific gravity . . . . | 1032·67 |
| Water . . . . . | 889·08 |
| Solid constituents . . . . | 110·92 |
| Sugar . . . . . | 43·64 |
| Casein and extractive matters . | 39·24 |
| Butter . . . . . | 26·66 |
| Salts yielded by incineration * . | 1·38 |

1. The age of the nurse does not exert any marked influence on the specific gravity, the proportion of water, or that of solids, unless when we contrast extremes, when we find that the milk of nurses aged from fifteen to twenty years contains much more solids than that of nurses aged from thirty to forty years.

The period at which the milk most nearly approximates to

* The relative proportions of the individual salts were as follows :

| | | | |
|---|---|---|---|
| Salts insoluble in water | 0·775, namely | carbonate of lime, | 0·069. |
| | | phosphate of lime, | 0·706. |
| Soluble salts, | 0·225 / 1·000 | chloride of sodium, | 0·098. |
| | | sulphate of soda, | 0·074. |
| | | other salts, | 0·053. |

See, however, the more minute analysis in the note to p. 285.

the physiologically normal type is for the ages of twenty to thirty years.

2 and 3. During the first fortnight the specific gravity of the milk is slightly diminished; there is a constant diminution in the quantity of water (resulting from an excess of butter), a diminution of sugar, and an augmentation of casein, butter, and salts.

The colostral state especially augments the quantity of butter.

The composition of the milk from the first to the twenty-fourth month presents the following varieties:—

There is no law regarding the variations of density.

The greatest quantity of water (901·51) occurs from the fifth to the sixth month; the least (872·92) during the first two months.

The sugar is in excess from the eighth to the tenth month (reaching 47·62), and is deficient during the first month (40·40).

The casein is in excess during the first two months (48·26), and is most deficient between the tenth and eleventh months (31·06).

The butter is in excess during the first three months, especially the first month, when it reaches 39·55.

The salts are most abundant during the first month, but present no regular law of decrease.

4. The composition of the milk in nurses of a weak constitution appears to be normal, while in nurses of very vigorous frame the weight of the solid portion is diminished.

5. The milk of a nurse with a first child more nearly resembles the physiological type than that of women who have borne many children.

6. Pregnancy in its later stages augments the amount of the solid constituents of the milk.

7. The state of development of the breasts does not exercise any marked influence on the milk.

8. The time during which the milk is retained in the breast does not seem in the case of women to exert any influence on the fluid, whereas in the cow and the ass the last-drawn portion yields very considerably more butter than the first-drawn milk. (See however, p. 277.)

9. The influence exerted by menstruation presents questions regarding which there have been great differences of opinion. Vernois and Becquerel only met with ten cases in which menstruation occurred during lactation, and in only three of them could they procure the milk both before and during menstruation.

The composition of the milk during menstruation appears to be modified as follows: — The density is diminished, the quantity of water sensibly diminished, the sugar slightly diminished, the casein somewhat augmented (once to 42·19), the butter much augmented in one case (to 67·74) and much diminished in another (to 10·67), and the salts slightly increased.

10. The milk of women with dark hair exceeds in quality that of women with light hair, approaching more nearly to the normal type in reference to each of its constituents.

11. The averages yielded by the milk of well-fed nurses closely approximate to the normal type. A deficient supply of food causes an augmentation of the water, due chiefly to the diminution of the casein and butter.

12. Where the state of health of the infant is satisfactory, the milk never deviates much from the normal type; when on the other hand the infant does not thrive, we usually find a low specific gravity and a considerable augmentation of the butter (rising as high as 33·22 in place of 26·66).

13. An excessive secretion of milk has no effect upon the specific gravity. The water, butter, and salts, are slightly diminished, and the sugar and casein somewhat increased. When the secretion of milk is scanty, the water and butter are in excess, while the sugar and the casein are diminished.

(251.) Vernois and Becquerel enter at great length into the consideration of the milk in various diseases. The following is a brief summary of their principal results. Milk in diseases.

In acute febrile diseases, such as enteritis, colitis, pleurisy, metro-vaginitis, and metro-peritonitis, the milk presents the following average composition;—

| | |
|---|---|
| Density | 1031·20 |
| Water | 884·91 |
| Solid constituents | 115·09 |
| Sugar | 33·10 |
| Casein and extractive matters | 50·40 |
| Butter | 29·86 |
| Salts | 1·73 |

Comparing this with the table in p. 280 representing the composition of healthy milk, we see that there is an augmentation of the solids collectively, and of the butter, the casein, and the salts individually, with a corresponding diminution of the sugar.

In typhoid fever, *all* the solid constituents of the milk occur in diminished quantities, excepting the casein which seems unaffected. The butter is especially diminished.

In chronic diseases without fever, the only peculiarities usually are a slight augmentation of the casein and a great increase of butter.

In pulmonary phthisis with diarrhœa and emaciation, the solids are considerably diminished, mainly owing to the great decrease of butter, which falls on an average to 12·76, and was once observed as low as 6·9.

In syphilis it appears from an examination of the milk in nine cases that the density is increased (in one case to 1037·5), the butter is diminished (on an average to 15·87, once to 9·12), and the salts are considerably increased. Antisyphilitic treatment by mercurials increases the quantity of butter.

The milk of animals.

(252.) The following table represents the composition of 1000 parts of milk in various animals, as deduced from the analyses of Vernois and Becquerel.

| | Density. | Water. | Solid Constituents. | Casein and Extractive Matters. | Sugar. | Butter. | Salts. |
|---|---|---|---|---|---|---|---|
| Woman - - | 1032·67 | 889·08 | 110·92 | 39·24 | 43·64 | 26·66 | 1·38 |
| The Cow - - | 1033·38 | 864·06 | 135·94 | 55·19 | 38·03 | 36·12 | 6·64 |
| The Ass - - | 1034·57 | 890·12 | 109·88 | 35·65 | 50·46 | 18·53 | 5·24 |
| The Mare - | 1033·74 | 904·30 | 95·70 | 33·35 | 32·76 | 24·36 | 5·23 |
| The Goat - | 1033·53 | 844·90 | 155·10 | 55·14 | 36·91 | 56·87 | 6·18 |
| The Ewe - - | 1040·98 | 832·32 | 167·68 | 69·78 | 39·43 | 51·31 | 7·16 |
| The Bitch - - | 1041·62 | 772·08 | 227·92 | 116·88 | 15·29 | 87·95 | 7·80 |

A full account of the analyses of the milk of these animals by other chemists may be found in the second volume of the translation of Lehmann's "Physiological Chemistry," pp. 341—343, and in Bouchardat and Quevenne's treatise, entitled "Du Lait en général. Des Laits de femme, d'ânesse, de chèvre, de brebis, de vache en particulier," Paris, 1857.

Daily quantity of milk.

(253.) The daily quantity of milk is dependent upon various conditions, such as bodily constitution, food, &c. During the earliest period of lactation the mammary glands secrete less milk than subsequently, the secretion attaining its maximum four or five days after delivery. Lampérierre determined the quantity of milk secreted in definite times by a large number of women, and found, as a mean for each breast, between fifty and sixty grammes in the course of two hours. Assuming that the secretion of milk proceeds at an equal rate during the twenty-four hours, a woman would discharge daily about 1320 grammes, or rather more than forty ounces (by weight). Estimating the average weight of a woman at about 134 lbs., there would be 2·2 lbs. of milk secreted daily for every 100 lbs. weight of the body.

A cow, according to the experiments of Boussingault, yields on an average about six kilogrammes of milk daily, and, since on an average a cow weighs 580 kilogrammes there are 1·04 parts (by weight) of milk for every 100 parts

(by weight) of the cow. Hence, if we know the weight of the cow, we can at once calculate the average quantity of milk that she ought to yield.

Origin of milk.

(254.) With respect to the origin of the milk we need only here remark that none of its leading constituents have been recognised in the blood. We have already shown (p. 106) that the reactions, from which it has been inferred that casein exists in the blood, afford no certain proof that such is the case; and the same remark holds good with regard to the milk-sugar, for both the sugar occurring in the blood and inosite (or muscle-sugar) differ essentially in their physical and chemical characters from milk-sugar. Although it is possible that the fat may pass by transudation from the blood into the milk, we have no evidence that such is the case, and we know that cholesterin, which traverses very readily through some sets of capillaries, does not occur in the milk; further, it is very questionable whether the butyrin exists in normal blood. Moreover, the salts do not pass into the milk in consequence of simple transudation, for on comparing the salts of a transudation with those of the milk, we find that the chlorides do not preponderate to nearly so great an extent in the latter as in the former, while the potassium compounds and phosphates are present in the milk in even larger quantities than in the blood-corpuscles.*

* The following comparative analyses (by Weber), of the ashes of cow's milk and ox-blood distinctly show the above mentioned relations.

| | Cow's Milk. | Ox-Blood. |
|---|---|---|
| Chloride of potassium | 14·18 | none. |
| Chloride of sodium | 4·74 | 38·82 |
| Potash | 23·46 | 11·44 |
| Soda | 6·96 | 29·09 |
| Phosphoric acid | 28·40 | 7·74 |
| Lime | 17·34 | 1·90 |
| Magnesia | 2·20 | 0·75 |

# CHAPTER XIII.

## THE SECRETIONS OF THE MUCOUS MEMBRANE AND THE SKIN.

### SECTION I. — MUCUS.

Mucus.

(255.) The term *mucus* has a somewhat vague signification: it includes not only the secretion of true mucous membranes, but also (1.) the contents of certain cysts occurring in the thyroid gland, the liver, the kidneys, and the ovaries (which, according to Virchow and Rokitansky, yield all the reactions characteristic of pure mucus); (2.) the gelatinous matter of the umbilical cord (which readily becomes converted into mucus); and (3.) the contents of certain serous sacs, as for instance the synovial membranes.

Its physical characters.

Mucus in its normal state occurs as a tough mass, capable of being drawn up in threads, consisting of a clear viscid fluid containing a number of epithelial cells; but even perfectly normal mucus may present many varieties of character, both in reference to its chemical reactions and its morphotic elements, according to the structure of the membrane from which it is secreted.

Its morphotic elements.

(256.) The epithelial cells occurring in mucus may either belong to the tessellated, the cylindrical, or the ciliated variety, and they are so abundant that it is often almost impossible to distinguish the intercellular fluid in which they are suspended.

Mucus-corpuscles.

Mucus-corpuscles, which are very similar to the colourless blood-cells and to pus-corpuscles, are always present in normal mucus, although frequently only in very small numbers. In

inflammatory conditions of the mucous membrane they increase to such a degree that, when examined under the microscope, the mucus seems to be entirely composed of these bodies.

Fibrinous coagula, associated with blood-corpuscles, are constantly found in exudative or croupous inflammations of the mucous membranes.

Granular cells.

In the mucus of the air-passages we often find the so-called inflammatory globules or granular cells. They may occur towards the close of a croupous inflammation, or altogether independently of it; as for instance in the thick tenacious mucus which is expectorated in the chronic bronchial catarrh of aged persons.

Fat occurs in almost every kind of mucus, either in the form of globules or of very minute granules: its quantity is much increased in catarrhal affections.

Molecular granules are seldom entirely absent, and are especially abundant in constitutional diseases, such as tuberculosis, cancer, and typhus.

Vibriones and microscopic fungoid growths occur only in mucus in which a process of decomposition is commencing.

Its chemical constituents. Mucin.

(257.) The most important chemical constituent of mucus is mucin, which imparts to the mucus its most characteristic properties. It forms the basis of the mucus, and may be obtained by pounding and rinsing the salivary glands, the gelatinous matter of the umbilical cord (the gelatin of Wharton), or fœtal areolar tissue, with water. It does not coagulate on boiling, is precipitated, without re-solution, by acetic acid and by a solution of alum (the coagula produced by acetic acid appearing under the microscope as fibrinous threads), is precipitated, with re-solution, by the mineral acids, and is not thrown down from these mineral-acid solutions by ferrocyanide of potassium. It is distinguished from pyin (a substance which it closely resembles, and which will be described in the chapter "On Exudations"), in not being thrown down

by bichloride of mercury or neutral acetate of lead, and in being precipitated by basic acetate of lead. By prolonged boiling in sulphuric acid (one part of acid in four of water) it yields leucine and more than 4% of tyrosine. The only trustworthy ultimate analysis of mucin is due to Scherer, who found as the mean of three experiments: —

| | |
|---|---|
| Carbon . . . . . | 52·10 |
| Hydrogen . . . . . | 6·97 |
| Nitrogen . . . . . | 12·82 |

and, therefore,

| | |
|---|---|
| Oxygen . . . . . | 28·11 |

No sulphur was present, but there was more than 4% of white ash, which, in addition to much phosphate of lime, contained some alkaline carbonates.

Albumen. Albumen is not present in normal mucus, but appears whenever the mucus membrane assumes an inflammatory state.

The extractive matters occurring in the mucus have not been carefully examined. They doubtless include the free acids which are frequently found in mucus, and with whose nature we are not acquainted. Indeed, Andral maintains that pure

Reaction of mucus. normal mucus is always acid; but although this assertion may be true, it has not been proved to be so. All that we know is that the ordinary secretions of the mucus membrane are sometimes acid and sometimes alkaline, and that probably the reaction is often due to the admixture of extraneous ingredients.

Salts. Chloride of sodium is the preponderating mineral ingredient of mucus; and, in addition to it, we find in the ash alkaline carbonates, a small quantity of alkaline phosphates and sulphates, and some earthy phosphates. The collective salts amount to about 0·7% of the mucus.

Water. The water in mucus ranges from 88·2 to 95·6%.

(258.) Two different theories have been propounded regarding the origin and formation of mucus. Tilanus * argues that wherever true mucus occurs we have a secreting or investing membrane (even in colloid cysts), which is covered with epithelium; and that further, we always find epithelium in mucus, and that hence there must be a causal connexion between the production of mucus and the formation of epithelial cells — in short that the cells must be formed from a mucin-containing blastema, or in other words, that the mucus is formed from the blood; the albuminates of the liquor sanguinis, becoming decomposed, under certain unknown conditions, into the structure forming the epithelial cells and into mucus. This view is opposed by Scherer, Virchow, Schrant, and Donders, who all agree that the mucus is the product of the cells, but who differ on minor points; the two former holding that the mucus is formed by the gradual solution of the cells, much in the same manner as the gastric juice is formed, while the latter regard the mucus as a product of the metamorphosis of the contents of the epithelial cells. There are no chemical grounds for preferring either of these theories to the other.

Origin of mucus.

## SECTION II.—SEBACEOUS MATTERS.

(259.) Under this general title we include not only the product of the sebaceous follicles, which are distributed over the entire skin, but likewise the secretions of the Meibomian and ceruminous glands, the smegma preputii, castoreum, and the vernix caseosa.

Sebaceous matters.

All these secretions abound more or less in morphotic elements, the matter yielded by the sebaceous follicles being especially rich in small epithelial cells. We also find in

The morphotic elements.

* De saliva et muco. Amstelodami, 1849, pp. 56—75.

these secretions, especially in the products of the Meibomian and ceruminous glands, peculiar oval or polyhedral cells, varying in diameter from $\frac{1}{200}$ to $\frac{1}{140}$ of a line; which in addition to a pale nucleus with nucleoli, contain minute dark, and clearly defined granules and a few fat globules. If the sebaceous follicles are in a state of inflammation pus-corpuscles will be found in their secretion.

Their chemical constituents.

A protein-substance, whose exact nature is not known *, occurs in all the above-named secretions. Lehmann found 4% of it in the vernix caseosa, 5·6% in the human smegma preputii (collected after several operations for phymosis), 2·9% in that of the horse, and 5·8% in Canadian castoreum.

Neutral fats occur abundantly in these substances. In the vernix caseosa Lehmann found 26·2%, in human smegma preputii 47·5%, in that of the horse 49·9%, and in Canadian castoreum 8·2%.

No volatile fatty acids have been detected in any of these secretions.

An ammonia-soap is found in the smegma preputii, which also contains a little cholesterin.

These substances contain only a small amount of mineral constituents, namely, a little chloride of sodium, and hydrochlorate of ammonia with phosphate of soda and ammonia. Earthy phosphates, on the other hand, are present in considerable quantity, amounting, according to Lehmann, to 6·5% in the vernix caseosa, 9·5% in the preputial secretion of man, and 5·4% in that of the horse.

The water must naturally vary much in this class of secretions; Lehmann found 66·98%, and Dr. John Davy 77·87% in the vernix caseosa.

(260.) A few substances still require notice, which must be

* Being of necessity separated in an insoluble form from the fatty matters with which it is associated, we cannot determine whether it is most similar to albumen or casein. Its behaviour with acetic acid and ferrocyanide of potassium, with strong nitric acid, &c., show that it is a protein-substance.

regarded either as accidental admixtures or as constituents peculiar to individual secretions.

Thus alcohol takes up from castoreum a resinous constituent which contains carbolic acid, or hydrated oxide of phenyl ($C_{12}H_5O.HO$), as may be shown by the blue colour which it imparts to a pine shaving saturated with hydrochloric or nitric acid * (see p. 80). Castoreum.

Salicylous and salicylic acids, probably derived from the willow-bark on which the animal feeds, are also found in castoreum (Weber).

The preputial secretion of the horse and castoreum contain hippuric and often benzoic acids.

In fresh castoreum we can recognise with the microscope crystals of sulphate of lime and in the preputial smegma of the horse crystals of oxalate of lime.†

* Lehmann observes, that as the resinous constituents of castoreum coincide remarkably with those of hyraceum (which he believes to be the dried intestinal excrement of Hyrax capensis, and not a urinary product, as was formerly supposed), and as carbolic acid occurs in both these substances, it seems most probable that they are not products of the metamorphosis of tissue, or that they are any peculiar secretion, but merely derivatives of the resinous substances occurring in the food.

† In connexion with the subjects noticed in this section, we may allude to the peculiar secretions yielded by the cutaneous glands of certain reptiles. These glands in Lacerta salamandra yield, according to Gratiolet and Cloez, a white fluid of the consistence of rich milk, which very rapidly coagulates ; it has an acid reaction, and an acrid and repulsive odour. Birds, mice, and guinea-pigs, when inoculated with it, were attacked with convulsions, but seldom died. The secretion of Rana bufo (the common toad), appears to possess similar but more powerful properties ; birds when inoculated beneath the wings, dying in five or six minutes without convulsions, even after the matter had been dried and mixed with an alkali, an apoplectic effusion being found in the cerebellum. Dr. John Davy, by pressing the cutaneous follicles of the same reptile has obtained a thick fluid, of which the part soluble in water and alcohol yielded on evaporation a pale yellow neutral substance, which on application to the skin excited pain, fused on being heated, but did not give off any ammoniacal odour, and dissolved in nitric acid with a purple colour. Hautz has examined the fluid which Bufo cinereus can eject from the cutaneous glands, when irritated. He found that it was alkaline, and that the greater part of the solid residue, which did not exceed 0·5%, was urea. No uric acid could be detected. The above brief and incomplete notices show that the subject requires further

## SECTION III.—THE SWEAT.

The sweat.

(261.) The sweat as it exudes from the open mouths of the ducts of the sudoriparous glands, and collects upon the skin of a person who is perspiring freely, is, as is well known, a colourless and very watery fluid, with a rather saltish taste, and usually evolves a very characteristic odour, which varies with the cutaneous surface from which it has exuded. It normally has a faintly acid reaction; but sweat that has been collected from the axillæ or from the feet is often found to be alkaline.

The best method of collecting sweat for chemical examination is that adopted by Schottin and Funke. The arm (the organ most conveniently operated on) is enclosed in a tolerably loose caoutchouc sleeve, which grasps the limb tightly above, while below it communicates with a small flask in which the fluid collects.

Its morphotic elements.

Normal sweat usually contains a considerable amount of epithelium, which gives it, when viewed in large quantity, a turbid, almost milky appearance. According to Funke the epithelium ranges from 0·191 to 0·307% of the sweat, and it seems to be increased in a direct ratio with the intensity of the secreting action.

Its chemical constituents.

The solid non-volatile constituents of sweat range from 0·7 to 2·6% (Funke). The chlorides of sodium and potassium make up more than half of this solid residue.

Neither alkaline phosphates nor ammonia-salts occur in the sweat; but ammonia is rapidly developed in decomposing sweat. The earthy phosphates and peroxide of iron, which always occur in the ash, are due solely to the epithelium.

investigation. An examination of the secretion of the anal glands of the pole-cat, skunk, &c., might also lead to very interesting results. I am not aware that any chemist has yet ventured on the task.

According to Funke the salts vary from 0·246 to 0·629% of the fluid.

Although some of the fat contained in the sweat is due to the sebaceous follicles, a portion is undoubtedly yielded by the sudoriparous glands; for the sweat obtained from the palm of the hand, which contains no sebaceous glands, always contains a little fat.

Fatty acids.

Volatile fatty acids form the principal part of the organic matters held in solution in the sweat. Lehmann has proved that these acids originate from the sweat-glands by showing that the fat of the sebaceous glands, when saponified, yields hardly a trace of them. Of these acids the most abundant is formic acid, while there is a smaller quantity of acetic acid and still less of butyric acid. The presence of metacetonic and capric acids is also probable, but has not been definitely proved.

Lactic acid.

Lactic acid, which was long regarded as an ingredient of sweat, does not exist in that fluid. A peculiar nitrogenous acid, termed hydrotic or sudoric acid ($C_{10}H_8NO_{13}$) has been described by Favre * as occurring in sweat, but its existence is very doubtful.

Urea.

Urea occurs in small quantities in the sweat, and in some renal affections, especially in uræmia, is very abundant, especially in the sweat of the face. Funke has carefully studied the relations of urea to the sweat, and has ascertained that, as in the case of the urine, the quantity of urea is dependent to a certain degree on the quantity of water that is yielded by the sudoriparous glands, and that after prolonged sweating the quantity of urea in the sweat is much diminished. In one experiment he found that the sweat yielded by the whole body in one hour was 215·067 grammes or nearly 7 ounces, and that it contained 0·423 of a gramme, or about

* As Favre entirely overlooks the existence of volatile acids in the sweat, and as he determines quantitatively the lactic acid which, as Schottin, Funke, and others have proved, does not occur in sweat, we may well have doubts regarding his new acid.

7·5 grains of urea; this would be at the rate of 180 grains in a day if the sweating continued uniformly. In another experiment (both were made upon himself) the sweat in one hour amounted to 561·765 grammes or nearly 18 ounces, containing 0·629 of a gramme, or 9·7 grains of urea; if the secretion went on at this rate for twenty-four hours nearly half an ounce of urea would be given off daily by the skin. The quantities found by Funke considerably exceed the amount previously found by Picard and other observers.

Uric acid.

Uric acid is reported to have been found in the sweat in two or three cases (Wolf, Hamernjk). Schottin could find no trace of it in uræmic sweat, and even its occasional presence is doubtful.

Sugar.

Sugar has been detected in the sweat in cases of diabetes by several good chemists, while others (Hoefle and Lehmann) have sought in vain for it. With the view of seeing whether sugar would pass from the digestive organs into the sweat, Schottin swallowed more than a pound of milk-sugar in thirty-six hours; the whole of the sweat collected in six hours yielded, however, no trace of sugar.

Pigments.

We know little or nothing with certainty regarding the colouring matters occurring in the sweat. Schottin often extracted a bright red colour by means of alcohol. In jaundice the bile-pigment sometimes enters the sweat and communicates a yellow tint to it.

The passage of various substances into the sweat.

(262.) Schottin has instituted various experiments regarding the passage of certain acids, salts, &c., into the sweat, and finds that tartaric, succinic, and benzoic acids pass in the course of five hours into the sweat, while iodide of potassium, taken daily to the extent of half a drachm, could not be detected in that fluid till the fifth day. Neither salicin nor quinine re-appeared in the sweat. After the ingestion of cinnamic acid, either its salts or those of benzoic acid (but which of the two Schottin could not determine) occurred in the sweat. The salts of tellurium, when taken internally,

communicate to the cutaneous excretion the fetid odour peculiar to those substances.

Certain gases, especially carbonic acid and nitrogen, are simultaneously exhaled with the liquid secretions of the sudoriparous glands; the ratio in which the above-named gases are excreted is variable, but most commonly about two volumes of carbonic acid are excreted for one volume of nitrogen.

Its amount.

(263.) The amount of the sweat has been more accurately determined by Funke than by any previous observer. In twenty-two experiments on himself and two of his students (each experiment ranging from one to two hours) he found that the quantity of sweat secreted by the whole body in one hour varied under different conditions (from quiet movement in a room to violent exercise in the sun) from 53 to 815·3 grammes (or from 13·5 drachms to 25·5 ounces); the maximum and minimum quantity of solids contained in it being 0·923 and 6·967 grammes, or from 14 to 107 grains. He found, as indeed common experience shows us, that the amount of sweat varies very much in different persons exposed to the same external conditions: thus, for instance, in two sets of parallel experiments on himself and two of his students, the relative quantities of sweat in an hour were 1 : 2·3 ; 4·4, and 1 : 1·7 : 2·06.

# CHAPTER XIV.

## THE URINE.

The urine.

(264.) THE urine is a fluid which is secreted by the kidneys from the blood, and it is the principal means through which the soluble *débris* of the organism, especially the nitrogenous and saline matters, are eliminated from the system. It is a very complex fluid, and its composition varies very considerably in different classes of animals. We shall, in the first instance, confine our remarks to the urine as it occurs in man.

Its general properties.

Healthy human urine, when freshly passed, is a clear fluid of a bright amber colour, a bitter saltish taste, and a peculiar aromatic odour. It is always heavier than water, its ordinary specific gravity ranging from 1·015 to 1·025, and in a state of health it probably never exceeds 1·030. Its normal reaction is acid, but the degree of acidity varies considerably.

(265.) If urine is placed in a perfectly clean vessel it does not exhibit any great proneness to decomposition. As it cools it generally deposits a slight cloudy sediment, which sinks very slowly, and is most obvious in the morning urine, which has been retained for some time in the bladder. After

Acid fermentation.

standing for some days exposed to the air at an ordinary temperature, we find that its reaction becomes more acid, and red or yellow crystals of uric acid, visible to the naked eye, are deposited in the mucous sediment and on the walls of the vessel; and the urine will often remain in this condition for weeks without further decomposition. If the urine is of low specific gravity, or if the temperature is higher than usual, this acid fermentation is rapidly replaced by another

decomposition, in which the fluid is first covered with a thin, glistening, and often iridescent pellicle, fragments of which gradually break off and sink to the bottom. The mucous sediment then becomes interspersed with dirty yellowish-white flakes; the urine becomes paler, assumes an alkaline reaction, and begins to develope a fetid ammoniacal odour. The red or yellow crystals are now replaced by white amorphous granules and colourless strongly refracting prismatic crystals of phosphate of ammonia and magnesia (triple phosphate).

Its morphotic elements.

(266.) The morphotic elements of the urine are comparatively few. Indeed, healthy urine, when freshly passed, presents merely a few scales of pavement epithelium derived from the mucous coat of the bladder. Urine, however, that has stood for some time, or that deviates from the normal type, may present, as organic morphotic constituents, mucus- and pus-corpuscles, cylindrical casts or tubes, spermatozoa, blood-corpuscles, coagula of fibrin, and certain fungi and infusoria, while the unorganised constituents are the urates, uric and hippuric acids, phosphate of ammonia and magnesia, earthy phosphates, oxalate of lime and cystine. We postpone the consideration of these sediments till we have discussed the general chemistry of the urine.

Urea.

(267.) The most important constituent of the urine is urea, a substance which we have already so fully considered that little remains to be added here.

Since the earlier part (pp. 37—49) of this volume was printed, additional observations, confirmatory of those of Lehmann, Beigel, &c., have been made in reference to the influence of diet on the excretions of urea.

Thus Warncke * (as a preliminary to his researches on the amount of urea excreted in typhoid fever) ascertained that

* See his Essay "On the Amount of Urea-excretion in Typhoid Fever." Translated from the Danish by Dr. W. D. Moore, and published in the Dublin Medical Press, 1859, vol. xlii. pp. 49—52 and 65—69.

the average quantity of urea eliminated in twenty-four hours is —

| | | | |
|---|---|---|---|
| For an adult man upon | mixed diet | 33·7 | grammes |
| „ „ | vegetable diet | 25·3 | „ |
| „ woman upon | mixed diet | 26·8 | „ |
| „ „ | vegetable diet | 20·1 | „ |

These are the average results of seven examinations for each individual.

Similarly Professor Haughton finds that "well-fed, flesh-eating, wine-drinking men" yielded, on an average, 576 grains (or 37·4 grammes), while "well-fed, water-drinking vegetarians" yielded only 394 grains (or 25·6 grammes).

Recent observations by Genth and others show that the quantity of urea increases with the quantity of water that is carried off by the kidneys. Thus, for example, if a man passes 1000 grammes of urine daily, containing 33 grammes of urea, he will pass about 42 grammes, if the quantity of his urine is raised to 2000 grammes, by copious water-drinking, and about 50 grammes if the urine rises to 3000 grammes.

Urea in diseases.

To the remarks which have been previously made (see p. 45) on the influence of disease in modifying the amount of urea we may add the following. In intermittent fevers it has been found (by Moos, Traube, and Redtenbacher) that, during the paroxysm, the secretion of urea and of urine generally is absolutely increased, while in the period of intermission there is a diminution both of the urea and of the urine generally. In the cold and hot stages about 3·5 times, and in the sweating stage about 0·5, more urea are secreted than in the period of intermission.

Urea in typhoid fever.

Warncke's investigations in reference to typhoid fever are of such importance that we shall borrow freely from his memoir. "The urine of a patient labouring under typhoid fever is not distinguishable by external characters from any

other. It may be pale, may be excreted in large quantity, and may be clear or may be turbid, opaque, deposit a copious sediment, and be secreted in small quantity (which is particularly the case in the commencement of the disease); but its special characteristic is that it contains *an absolute and relative increase of urea.*

This property is retained by the urine through the stages to which the disease may be said to increase; when, on the contrary, the latter diminishes, the amount of urea is likewise lessened, and the quantity continues smaller after the end of convalescence, until the restitution of the body is completely effected.

The following table exhibits the average numbers of more than fifty investigations (on thirty men and twenty women), which were repeated daily during the stay of the individuals in the hospital: —

| | Males. | Females. |
|---|---|---|
| In the first week | 43·2 grammes | 34·0 grammes |
| „ second „ | 39·9 „ | 30·2 „ |
| „ third „ | 30·9 „ | 24·1 „ |
| „ fourth „ | 23·2 „ | 20·5 „ |

If these numbers be compared with those representing the quantity of urea which is normally excreted, especially under the use of vegetable food, and there are very few patients that use even it, it must be allowed that increase of the quantity of urea is a constant phenomenon in typhoid fever. This character, however, is not peculiar to typhoid fever, for in many other acute diseases, as in pneumonia, pleurisy, rheumatic fever, &c., the quantity of urea is increased; but in all these the other organic constituents of the urine are simultaneously augmented, while this takes place with the urea in a less degree. We cannot attach too much importance to this circumstance. An increased quantity of organic matters in general indicates an augmented supply of combustible materials; but an increased quantity of urea without

any simultaneous augmentation of the other organic compounds in the urine, as is the case in typhoid fever, points, on the contrary, to a more energetic combustion." Warncke goes on to show that the increase of the quantity of urea is not equally great in all typhoid fevers, and that it varies directly with the height of the temperature, the rapidity of the pulse, and the degree of emaciation.

A diminution of the quantity of urea, though never to a degree below the normal standard, occasionally (but only seldom) took place; it was especially observed after violent hæmorrhage from the bowels, and when there was considerable enlargement of the spleen.*

In many cases the patients, during the entire course of the disease, took food regularly; but in none of them was the consumption of food followed by an increased quantity of urea.

Warncke lays great stress on the value of the determination of the urea in reference to differential diagnosis. "When I find," he observes, "the increase of urea without any augmentation of the other organic constituents of the urine to be peculiar to typhoid fever, I am easily led to seek in this fact a diagnostic sign between this affection and the diseases which in other symptoms resemble it, especially gastric fever and meningitis."

In gastric fever.

In gastric fever he found that the quantity of urea was not very different from what is excreted by healthy persons when

* Warncke connects the enlargement of the spleen and the diminution of the urea in the following manner. He holds Fuhrer's view (see p. 47), that the urea is derived from the blood-corpuscles, and believing that the spleen is the organ in which the blood-corpuscles should be changed into urea and uric acid, he maintains that the augmentation of the volume of the spleen in these cases is due to the proper metamorphosis not taking place, and to the consequent accumulation of blood-corpuscles in that organ. In his investigations regarding the function of the spleen, he arrived at the singular fact that although dog's urine never contains uric acid, this substance occurs in the spleen of that animal.

living on a vegetable diet. From an extended series of analyses he obtained the following mean numbers: —

| | Males. | Females. |
|---|---|---|
| For the first week | 22·1 grammes | 18·0 grammes |
| „ second „ | 24·2 „ | 19·8 „ |
| „ third „ | 25·7 „ | 20·4 „ |

Thus we have here the reverse of what occurs in typhoid fever. The quantity of urea is less in the first weeks than during convalescence.

In meningitis the differences in relation to the amount of urea are at least equally marked, according to Warncke. In a boy aged seven years, who died from meningitis, the mean daily quantity of urea was 6·4 grammes, while in a boy aged eight years, who died from typhoid fever, the minimum quantity of urea was 11·9 grammes. Heller (see p. 45) mentions meningitis as a disease characterised by an excessive excretion of urea. If Warncke's views are correct, it is possible that in Heller's cases there was an error in diagnosis.* In meningitis.

In diabetes there seems (from the investigations of Thierfelder and Uhle) to be a definite ratio between the daily quantity of nitrogenous food and the daily excretion of urea. In diabetes.

The modes of testing for urea have been fully described in pp. 38—41. Attempts have been made to calculate formulæ connecting the percentage of urea in urine with the specific gravity; even the best give only rough approximations to the truth.†

* Heller does not stand unsupported in his statement regarding the excess of urea in meningitis. Moos relates the case of a man with meningitis, in whom the daily urea (the average of five days) amounted to 41·2 grammes.

† Professor Haughton has given a diagram representing *the curve of urea* in man, in cases in which neither albumen nor sugar is present. If $x$ represent the excess of the specific gravity above 1000, and $y$, be the number of grains of urea in a fluid ounce of urine, its equation is $(28-x)^2 = 28(14-y)$, which shows that it is a parabola. Let (for example) the specific gravity be 1·018, then $x=18$, and the equation gives us $y = 10·5$ grains. He considers the

Uric acid.

(268.) Uric acid is for the most part in combination with soda, and exists in normal human urine in only very small quantity, seldom forming more than 0·1%. An adult usually discharges from 0·3 to 0·9 of a gramme daily, the most common quantity being about half a gramme or seven or eight grains.* Although the amount of uric acid does not vary with the nature of the food to the same amount as that of the urea, yet the nature of the diet does to a certain extent modify its quantity. Thus, for instance, Professor Haughton found that the mean daily quantity of uric acid excreted by beef-eaters and wine-drinkers was 4·5 grains, the maximum being 11·9 grains, and the minimum 0·7 of a grain, while vegetarians yielded on an average only 1·48 grains, part of which was hippuric acid. His investigations on this subject led him to the rather startling view that "no uric acid whatever should occur in the urine of man in perfect health, but that all the nitrogen of the urine should pass off in the form of urea, a more highly oxidated product than uric acid." There are several facts which support this view, amongst which we may notice, first, that of the urine of the dog containing no uric acid while that substance occurred in the spleen (see p. 300); and, secondly, that there is certainly no fixed proportion (although they generally occur in an inverse ratio) between the quantities of uric acid and urea. Ranke, for instance, found the ratio to vary from 1 : 50 to 1 : 80. The excretion of this substance seems to have no definite connection

following bed-side rule sufficient for ordinary purposes: "Half the excess of the specific gravity of urine (not containing either sugar or albumen) above 1000 is the number of grains of urea per fluid ounce."

* Kaupp found that on a mixed diet, and taking little exercise, he excreted, on an average, 0·519 of a gramme; Genth found, under similar conditions, that he excreted, on an average, 0·565; Neubauer found 0·28 as an average of five days, on two healthy men, and 0·49 as an average of eight days; and Ranke found 0·629 as a mean of twenty observations made upon himself; these give a daily mean of about half a gramme, or between seven and eight grains of uric acid.

with the age, sex, or weight of the patient, and not much even with the food. We have shown (see p. 8) that there are good reasons for attributing the presence of oxalic acid in many cases to imperfect oxidation of the blood. Similar reasons seem to apply here; and they are supported, to a certain extent, by Dr. Hammond's experiments described in p. 66, and by the other facts mentioned in the same paragraph. In addition to the general remarks in p. 67 on the conditions of the system which give rise to an augmentation of the uric acid, we may mention that it is constantly increased in leucæmia accompanied with enlargement of the spleen, in intermittent fever on the days of the paroxysms, and for some days after the attacks have ceased (Ranke). In chronic gout the quantity of uric acid in the urine is much diminished, the total average of all Dr. Garrod's analyses in these cases being far under a single grain*; in acute gout the daily excretion of uric acid is not necessarily increased, and indeed is often much diminished; in seven cases detailed by Dr. Garrod the total average of all the analyses was 3·62 grains.†

Augmentation of uric acid.

Genth has made the following singular observation regarding the influence of water (taken as a drink) on the excretion of uric acid. Living on his ordinary mixed diet and not drinking much water he excreted daily 0·324 of a gramme of uric acid; living on the same food and drinking 1000 c. c., or about 35 fluid ounces of water, he excreted only 0·396 of a gramme; drinking 2000 c. c., or about 70 ounces of water, he excreted mere traces; and when drinking 4000 c. c., or 140 ounces of water, he excreted no uric acid whatever; in these experiments the urea rose in an inverse proportion from 46·6 grammes to 52·1 grammes.

Influence of water,

According to Ranke, sulphate of quinine has a marked influence in checking the excretion of uric acid. As a mean of

of quinine.

* On the Nature and Treatment of Gout. London, 1859, p. 175.

† Op. cit. p. 163.

20 experiments he found that 20 grains of quinine reduced the uric acid of the succeeding 24 hours from 0·629 to 0·271 of a gramme.

Its microscopical characters.

The microscopic characters and the chemistry of uric acid have been already sufficiently noticed in pp. 63—65. We will merely add a description of the best method of determining the amount of this constituent in urine. Hydrochloric, nitric, or acetic acid may be used to precipitate the uric acid from the urine. If the urine contain no albumen nitric acid is preferable to hydrochloric, because uric acid is less soluble in the former than in the latter, and because the latter is believed to favour the acid fermentation, and the development of minute fungoid growths which tend to decompose the urates. Dr. Thudichum recommends that after the acid has been added, the urine shall be exposed to a temperature of 98° F. (on a sand-bath, for instance), which has the double advantage of forming much larger crystals than are produced at an ordinary temperature, and of preventing the deposition of any urates, which are not so easily acted upon by the acid as when they are in solution. The mixture should stand for from twenty to forty-eight hours, after which the crystals may be collected, washed, and weighed on a filter whose weight has been previously determined.

Hippuric acid.

(269.) Hippuric acid is now ranked amongst the ordinary constituents of healthy human urine.

We may here add a few remarks to the description we have already given (pp. 57—59) of the occurrence of this acid in the system; essays upon hippuric acid having been recently published by Weissmann and Hallwachs.

From observations made upon himself Weissmann is led to the conclusion that the hippuric acid which occurs in human urine is in part a product of the metamorphosis of the tissues, and is in part formed directly from certain kinds of vegetable foods (whose exact nature however he has not determined).

He always found hippuric acid in his urine, and more was

present during a mixed diet than when he lived on a purely animal diet (of fifteen eggs and a pound of meat daily). That it is formed independently of vegetable food is obvious from its occurring in the urine of typhous patients, (who during the preceding fortnight, or even month, had taken nothing but milk and broth,) in about the same quantity as in his own urine during an animal diet. On a mixed diet, he excreted daily 2·17 grammes, or 33·4 grains, and on a purely animal diet, only 0·79 of a gramme or 12 grains. It is probable that these numbers are much higher than would be generally found. Several years ago I made numerous analyses in reference to this constituent, but never, unless after the ingestion of benzoic acid, found such an amount in healthy urine as that given by Weismann. Duchek and Höfle deny that hippuric acid is a constant constituent of human urine, and Professor Haughton only met with it once in the urine of ten men, and in this case the fluid had a remarkable smell, compounded of that of sweet hay and apple-juice.

Weismann found that the quantity of hippuric acid was diminished in febrile diseases, pneumonia, intermittent fever, and in three cases of diabetes. He ascribes the diminution in the febrile cases to the abnormal rapidity of the metamorphosis of the tissues, and to an increased excretion of carbon by the lungs, while in the cases of diabetes he refers it to the exclusive animal diet: his observations are however in direct opposition to those of Lehmann, who found an excess of hippuric acid both in diabetes and in fever.

Kühne* has established the singular fact that no traces of hippuric acid can be detected in the ordinary urine in jaundice. Even when benzoic acid was given to jaundiced patients, or to dogs to which jaundice had been artificially induced, no hippuric acid, but only benzoic acid, appeared in the urine.

* Contributions to the Pathology of Icterus; translated in Beale's Archives of Medicine, vol. i. pp. 342—352.

Hallwachs has especially devoted his attention to the origin of the hippuric acid in the herbivorous animals. He first ascertained that grass and hay contain not only no benzoic acid, but no member of the benzoyl series that could produce benzoic acid in the system, and which by conjugation with glycine could yield hippuric acid, and he afterwards found that neither cumarin nor chlorophyll is converted in the system into hippuric acid. Hence he was led to the view regarding its origin which is propounded in p. 59, and which is further strengthened by recent experiments of Städeler on the gradual oxidation of albuminous substances.

The best method of searching for hippuric acid in human urine, is to evaporate three or four ounces of the fluid in the water bath to the consistence of a syrup, to extract the residue with alcohol, and to filter. The solution thus obtained contains the hippuric acid with urea, &c. We add a little oxalic acid to fix the urea, evaporate to the consistence of a syrup, and extract the residue with ether containing a little alcohol. The ethereal solution which contains the hippuric acid must be evaporated nearly to dryness, boiled with water, and filtered while hot. On cooling, or by slow evaporation, we get the acid in its characteristic crystallised form (*Plate III. fig.* 1).

Xanthine.

(270.) Xanthine now deserves a fuller notice than it received in p. 50. Since the earlier part of this volume was printed, it has been discovered by two excellent chemists, Scherer* and Strecker†, that xanthine is present, although in very small quantities, in normal human urine. Scherer has likewise found it in the brain, the spleen, the pancreas, and the liver of the ox; in the thymus gland of the calf; in the muscular tissue of the horse, the ox, and of fishes, as well as in the liver in acute yellow atrophy of that organ. According to Thudichum‡ it is a normal constituent of the human liver.

* Ann. d. Ch. u. Pharm. 1858, vol. cvii. p. 314.

† Ibid. 1858, vol. cviii. p. 151.

‡ Medical Times and Gazette, Dec. 4, 1858.

Uric acid, xanthine, and hypoxanthine form a closely allied physiological as well as chemical group. The two former occur simultaneously not only in the urine, but in the spleen, the liver, and the brain, while xanthine is not only invariably accompanied (according to Scherer) by larger or smaller quantities of hypoxanthine, but as Strecker has shown hypoxanthine can be made by the action of nitric acid to yield a product from which xanthine (in place of hypoxanthine) may be obtained by a process of reduction. Xanthine ($C_{10}H_4N_4O_4$) must be regarded as a higher stage of oxidation of hypoxanthine ($C_{10}H_4N_4O_2$) and a product of the regressive metamorphosis of the tissues, which in the ordinary condition of the system is excreted in a more highly oxidised form as urea, uric acid, &c.

The quantities in which xanthine occurs are so trifling, and the chemical difficulties of searching for it are so considerable, that we shall not attempt to describe its tests; and the same remark applies to the following substance.

Hypoxanthine.

(271.) Hypoxanthine (see p. 50) has been found by Scherer and Strecker to be constantly associated with xanthine, not only in the urine, but in almost all the animal fluids; in the blood, in the muscular tissue of mammals and fishes, in the juice of the spleen, kidneys, and liver, in the pancreas, the thymus and the thyroid glands, and the brain. Its chemical affinity to xanthine has been shown in the preceding paragraph. We are justified in inferring that hypoxanthine, which in pathological states is found in certain organs in large quantity, is in the normal condition of the organism converted for the most part into xanthine, which again is usually further oxidised into uric acid, urea, &c.

Allantoine.

(272.) Allantoine is a probable constituent of the urine in cases of impeded respiration (see p. 49). According to Schottin it occurs in the urine after large doses of tannin.

Creatinine and creatine.

(273.) Creatinine and creatine must be mentioned amongst the constituents of urine, although it is probable that the

latter may merely be a product of decomposition of the former yielded during the process of extraction.

The only observations on the amount of the daily excretion of these substances which (as far as I know) have yet been published, are those of Thudichum. Two men, each aged 28 years, and weighing between ten and eleven stone, were the subjects of the experiments recorded in the following table: —

| | Number of days observed. | Creatinine of 24 hours. | Creatine of 24 hours. |
|---|---|---|---|
| A | 5 | 9·66 grains. | 6·32 grains. |
| | 4 | 5·61 „ | 4·68 „ |
| | 5 | 6·00 „ | 3·67 „ |
| B | 2 | 6·31 „ | 4·77 „ |
| | 5 | 5·66 „ | 3·45 „ |
| | 5 | 8·76 „ | 4·36 „ |

Nothing is known regarding the excretion of these substances in disease.

Formic acid.

(274.) Formic acid is sometimes present in very small quantities in the urine of healthy persons (see p. 11). The administration of amygdaline to rabbits either into the stomach or directly by injection into the veins, causes this acid to appear in the urine in considerable quantity (Ranke).

Lactic acid.

Lactic acid is so commonly regarded as a normal constituent of the urine, and indeed so often actually occurs in that fluid, that although it is in reality only an abnormal ingredient, we shall notice it here. Lehmann has very carefully investigated this subject, and the conclusions at which he has arrived have been already given in p. 22 in our remarks upon "Lactic Acid." It has been proved by the investigations of Boussingault, Robin and Verdeil and others to exist in considerable quantity in the urine of the horse and cow, and in that of pigs when fed upon potatoes.

Butyric acid.

Butyric acid is sometimes found in small quantities both

in healthy and in morbid urine, especially in the urine during pregnancy, and shortly after delivery.

(275.) Trimethylamine, a basic body, homologous with ammonia, and in which the three equivalents of hydrogen of the ammonia are replaced by three equivalents of methyle, ($C_2H_3$) has been obtained by Dessaignes and subsequently by Buchheim from the urine, but it should probably be merely regarded as an accidental product of decomposition.* Trimethylamine.

(276.) Extractive matters, or, in other words, the collective substances of whose individual composition we have no accurate chemical knowledge, occur in the urine in very variable quantities; and they are usually increased in most diseases. They are doubtless somewhat indefinite products of metamorphosis of the tissues. They are, according to the researches of Scherer, excreted far less abundantly in reference to their weight, by children than by adults, children from 4 to 7 years for every thousand parts by weight yielding daily 0·156, while an adult yields 0·386.† In prolonged starvation the extractive matters of the urine are much increased, and exceed the urea in quantity. Extractive matters.

Included in these extractive matters are the damaluric acid and damolic acid (see p. 17), the hydrated oxide of phenyl (phenylic or carbolic acid) and the hydrated oxide of tauryl (or taurylic acid) (see pp. 80—81)—a series of volatile acids obtained by Städeler by means of distillation from the

* Hofmann, the discoverer of this volatile alkaloid or base ($C_6H_9N$), has shown that it exists in the brine of pickled herrings, to which one of its salts gives its peculiar flavour. He supposes that it is formed by some kind of putrefaction of an acrid compound contained in the fish. It has likewise been obtained by C. Schmidt from the alcohol-extract of the retina.

† Similar experiments which do not altogether confirm those of Scherer, have been made by Rummel, who found that a boy aged three years excreted 0·232 of extractive matters in twenty-four hours for 1000 parts by weight; a boy aged four years 0·294; a girl aged five years 0·410; a youth aged eighteen years 0·195; and a man aged sixty-five years 0·382. In both sets of experiments the extractive matters included mucus, uric acid, &c., in short everything solid but urea, and fixed salts.

urine of the cow, the horse, and man; and which, if they really exist in the urine and are not formed by chemical processes, are probably the main cause of the peculiar odour of the urine. Lehmann, however, does not believe that they exist preformed in the animal body.

Urine pigments.

(277.) The urine pigments have been carefully studied both chemically, and in relation to diagnosis, but with little profit in either direction. In addition to the remarks in pp. 98, 99, it should be mentioned that Schunck* has recently found indican (which seems to be identical with Heller's† uroxanthin in the urine). This indican is the name given to a gum-like mass obtained from the chromogen of Indigoferous plants; when boiled with acids it yields indigo-blue, a peculiar description of sugar, and some other matters. Schunck has obtained indigo-blue from the urine in so many cases that we are entitled to place indican amongst the normal constituents of the urine. Its quantity is however extremely small, for by working for several weeks on the urine of two persons Schunck only obtained one grain of indigo-blue. The urine was examined for this substance in forty different persons of different sexes and ages, and all of whom were apparently in good health, and in every instance except one it was detected. The amount seems to vary from a comparatively tolerable quantity to a mere trace. Diet had no apparent effect on its production; and the state of health and the appearance of the urine afford no indications regarding the presence of an excess or deficiency of this substance.

Indigo.

The urine of the horse and cow gave comparatively large quantities of indigo-blue, especially that of the horse.

* Memoirs of the Literary and Philosophical Society of Manchester, 1857, vol. xiv. p. 239.

† See the foot-note to p. 98, in which it may be mentioned that there is a misprint of Scherer for Sicherer.

The following are the general steps to be adopted in the search for this substance.

The urine having been mixed with basic acetate of lead until no more precipitate is produced, is filtered, and sulphuric acid is then added to it on the filter. After the precipitate has been washed with water the liquid is mixed with an excess of ammonia, which gives more or less of a white or yellowish-white precipitate. This precipitate is collected on a filter, slightly washed with water, and then treated with dilute sulphuric or muriatic acid in the cold. After the whole of the oxide of lead has combined with the acid employed the liquid is filtered. When there is much of the indigo-producing body present the filter acquires a blue tinge; small particles of blue pigment are seen dotting the surface of the sulphate or chloride of lead, and the surface of the liquid, which is of a brownish-purple colour, in a very short time becomes covered with a thin pellicle, which is blue by transmitted and copper-coloured by reflected light, particles of the same blue substance being at the same time found attached to the sides of the vessel. When there is less of the indigo-producing body present, this pellicle only appears after some time, sometimes not till the next day. After twenty-four hours, however, the action of the acid is always completed, so that if no indigo-blue then appears or can be detected on examination of the deposit the total absence of the indigo-producing body may be inferred.

Mr. Schunck, from whose memoir the above method is taken, believes that "the occurrence of the indigo-producing body as an excretion is due to a disproportion between the oxygen absorbed by the system and the matter to be acted on by it, which again may be caused either by an excessive waste of the tissues or by an obstruction of the organs conveying oxygen, as the lungs and skin, or, as is probably the case in the majority of instances, by an excess of food being taken over and above the requirements of the system." As regards the

constitution of this body, he thinks there can be no doubt that it contains the elements of indigo-blue and sugar, and that by oxidation within the system it is converted into the ordinary extractive matter of the urine, which contains, as he has ascertained, the elements of sugar and of the black substance which is formed by the action of strong acids on urine, and which may be considered as a product of the oxidation of indigo-blue. He thinks it probable that the indigo-producing body will be found, as regards its formation and composition, to occupy a place between the substance of the tissues and the ordinary extractive matter of urine. The formation of a substance containing the elements of indigo-blue in the animal system is a fact which may lead to important conclusions regarding the chemical composition of the complex bodies of which the blood and tissues consist.

Little or nothing is known regarding the chemical composition of the morbid colouring matters of the urine.

Mineral constituents.

(278.) In considering the mineral constituents of the urine we shall commence with the one which forms the greater part of the bulk of the ash, namely, the chloride of sodium.

Chloride of sodium.

The relations of this salt to the urine have been very thoroughly investigated by numerous observers.* Hegar, in 1852, published a series of observations on the subject. Experimenting upon eight students he found that the daily

* The following table gives the results of the most trustworthy observations on this subject.

| | Chloride of sodium in twenty-four hours. |
|---|---|
| Hegar (eight sets of observations) | 17·500 grammes |
| Buchheim (six „ „ ) | 11·300 „ |
| Wagner (six „ „ ) | 11·309 „ |
| Kaupp | 14·993 „ |
| Do. | 17·046 „ |
| Genth | 12·834 „ |
| Do. | 18·507 „ |
| Jul. Lehmann | 9·614 „ |
| Bischoff (mean of forty days) | 14·790 „ |

These figures show how much the quantity daily excreted of chloride of sodium may vary. They yield an average of 14·5 grammes.

average of chlorine varied in these individuals from 7·4 to 13·9 grammes, the general daily average being thus 10·46 grammes, which corresponds to 17·5 grammes of chloride of sodium. Vogel* considers this average too high, and regards from 10 to 13 grammes, or from 150 to 200 grains, of chloride of sodium as the normal average for an adult male, the quantities being smaller for women and children.

The influence of age and sex is exhibited in the following tabular view of Bischoff's observations on this subject.

| | | | | Urine. | Chloride of Sodium. |
|---|---|---|---|---|---|
| A man aged | 45 years, | weighing | 238lbs. | 53 fluid oz. | 14·79 grammes. |
| A woman aged | 43 „ | „ | 198 „ | 33 „ | 9·13 „ |
| A girl aged | 18 „ | „ | 146 „ | 25 „ | 7·46 „ |
| A youth aged | 16 „ | „ | 107 „ | 26 „ | 8·80 „ |

After prolonged fasting, or after the use of food deficient in chlorides, there is a diminished excretion of this salt. Wund found that on totally abstaining from salt for five consecutive days the quantities of chlorine which he excreted daily (and of course it is an accurate measure of the chlorides) were 7·2, 3·6, 2·4, 1·4, and 1·1 grammes respectively. Falck, on contrasting the quantities of chlorine in the urinary chlorides during diets consisting of non-salted and of salted food, found that in the former case the chlorine was represented by 2·6, 1·7, and 0·9 grammes, while in the latter case the numbers were 6·1, 7·9, and 10·3 grammes. Kaupp† has instituted a very careful series of comparative experiments regarding the amounts of ingested and excreted salt. They stand in a direct

* Die Semiotik des menschlichen Urines, p. 326; (being the second part of Neubauer u. Vogel's Anleitung zur qual. u. quant. Analyse des Harns. 3rd ed. 1858.)

† The following are some of Kaupp's mean numbers.

| | | | | | |
|---|---|---|---|---|---|
| On taking daily | 33·6 | grammes of salt | he excreted | 27·3 | grammes by the urine. |
| „ | 28·7 | „ | „ | 24·1 | „ |
| „ | 23·9 | „ | „ | 17·7 | „ |
| „ | 19·0 | „ | „ | 17·0 | „ |
| „ | 14·2 | „ | „ | 13·6 | „ |
| „ | 9·3 | „ | „ | 10·1 | „ |
| „ | 1·5 | „ | „ | 3·8 | „ |

ratio to one another, but the amount of the latter never reaches that of the former, unless the amount of salt taken is small. Similar experiments leading to similar results have been made by Wagner and Buchheim. Wagner shows by analysis that the missing chlorides are not contained in the fæces; they must therefore be mainly carried off in the sweat. From experiments made by Hegar, Kaupp and others, it appears that the excretion of chlorine reaches its maximum in the afternoon and its minimum during the night, rising again in the morning. The excretion of chlorine is increased by bodily exercise, by sleeplessness, and by mental activity (Hegar, Kaupp); by copious water-drinking (Genth, Bischoff) and by the free administration of liquor potassæ (Parkes). Tea, coffee, alcohol, and tobacco smoking cause a diminution in the excretion of the chlorides, doubtless by checking the general metamorphosis of the tissues (J. Lehmann, Böcker, Hammond).*

The amount of the excretion of chlorine (or of chloride of sodium) is very much influenced by certain conditions of disease.

Vogel concludes, from a very large number of observations, that in all acute febrile diseases the excretion of chlorine by the urine rapidly diminishes, and often attains a minimum not exceeding the hundredth part of the normal quantity. With incipient improvement we have an augmentation, and as convalescence advances the chlorine reaches or even exceeds its normal quantity.†

* I gladly avail myself of this opportunity to express my opinion of the great value of Dr. Hammond's physiologico-chemical researches, and at the same time to thank him for his courtesy in transmitting to me copies of his memoirs.

† The following cases are extracted from Vogel's work. It must be recollected that Vogel regards the normal daily excretion of chlorine to range from six to eight grammes.

(1) A man with severe pleuropneumonia. On the third day, the chlorine had fallen to 0·6, on the fourth day to 0·3, and on the following day to almost 0. It then steadily rose to 0·4, 1·8, 2·6, 5·5, and 9 grammes on successive days.

The diminution of the chlorine may be referred to several causes. (1.) It is doubtless considerably due to the loss of appetite, and to the comparatively saltless food taken by patients with acute diseases. (2.) Chlorides are often, in these cases, separated from the blood in other ways, as, for instance, by watery diarrhœa or by serous effusions; thus Beale found that, while in the stage of hepatisation of pneumonia the urine contained mere traces of salt, the sputa and pulmonary tissue contained it abundantly. (3.) It is possible that in these diseases the secreting activity of the kidney, in relation to this, as well as to some other urinary constituents, may be diminished.

From the preceding remarks it is obvious that we have possession, in the amount of the excreted chlorine, of an important diagnostic (or rather prognostic) indication, which may be thus laid down :—

In all acute diseases a persistent diminution of the chlorine indicates an increasing intensity of the disease, while a persistent augmentation of the chlorine indicates a diminished morbid action. If the daily chlorine is less than 0·5 of a gramme, there is probably intense morbid action, accompanied with anorexia and either watery diarrhœa or profuse serous exudation. In cases of recovery, when the chlorine returns to the urine, we can judge by its quantity regarding the improved state of the patient.

In chronic diseases the daily amount of the excreted chlorine forms a tolerably certain measure of the digestive

(2) A man with typhus. The chlorine rapidly sunk to a minimum, and for several days was almost 0. With convalescence it gradually but irregularly increased, till it reached the normal quantity.

(3) A woman with acute articular rheumatism and pericarditis. It fell during the height of the disease to 1, and gradually rose during convalescence to 6·3 grammes.

(4) A young man with severe febrile bronchial catarrh. It rapidly fell to 0·8, and then in the course of a few days rose to 10·6 grammes.

(5) An old man similarly afflicted. It fell to 1·1, and during convalescence, when food was freely taken, rose to 20·5 grammes.

powers of the patient. When from six to ten grammes are excreted, we infer that the digestion is good; when a smaller quantity than five grammes is excreted we infer that it is impaired, unless chlorine is being simultaneously carried off by watery stools, or the prescribed diet should be deficient in chlorides. A very increased excretion of chlorine is a favourable sign in cases of dropsy.

In the preceding remarks we have sometimes used the term chlorides, but in reality nearly all the chlorine contained in the urine occurs there as chloride of sodium.

Sulphates. Sulphates are always present in the urine, but apparently (as may be seen by the results recorded in the footnote)* in very varying quantity. Lehmann (in his "Handbuch") states that an adult man secretes daily 2·1 grammes or about 32·4 grains of sulphuric acid.

The urine of young children contains a comparative excess of sulphates (Lehmann).

The nature of the food and the period of digestion considerably affect the amount of the excretion of sulphates. During a twelve days' persistence on a strictly animal diet, Lehmann excreted as the mean amount 10·399 grammes of sulphates (not sulphuric acid), while the corresponding mean amount, during a purely vegetable diet, was only 5·846 grammes; and similarly, Clare, during a purely animal diet of three days' duration, excreted on an average 3·697 grammes of sulphuric

* The following are the most trustworthy results regarding the daily excretion of sulphuric acid, in the form of soluble sulphates.

| | Sulphuric acid. |
|---|---|
| Lehmann (mean of experiments on himself) . | 3·934 grammes. |
| Gruner (mean of experiments on 7 persons) . | 1·904 „ |
| Buchheim (mean of 12 experiments on himself) . | 1·741 „ |
| Wagner (mean of 10 experiments on himself) . | 2·105 „ |
| Neubauer (mean of 17 experiments on himself) . | 2·480 „ |
| Do. (mean of 22 days' experiments on another man) | 2·270 „ |
| Clare (mean of 14 experiments on himself) . | 2·280 „ |

If we omit Lehmann's result, which is obviously abnormally high, we obtain 2·13 grammes as the mean daily quantity of excreted sulphuric acid.

acid, and during a purely vegetable diet 1·559 grammes. Gruner found that during perfect abstinence the sulphuric acid of the first twenty-four hours was not diminished, but it is very improbable that this should be generally the case. According to Dr. Bence Jones there is a temporary augmentation of the sulphuric acid shortly after every meal. Gruner and Beneke found that the curve representing the secretion of this acid rises during the afternoon hours (the period of digestion), sinks during the night, and reaches its minimum in the forenoon. According to Dr. Parkes, the sulphuric acid in the urine goes on rising for three hours after a meal, and continues increasing for three hours more. Copious water-drinking increases the daily amount of the excreted sulphates *, so also do strong bodily exercise, and great mental excitement. The sulphates of the alkalies when taken in considerable doses, are entirely eliminated in from eighteen to twenty-four hours, unless when a portion of them passes off with the solid excrements; and after the administration of large doses of free sulphuric acid and of sulphur, as also after the ingestion of golden sulphide of antimony in five-grain doses, four times daily, the excretion of sulphuric acid is temporarily augmented.

From the above remarks it is obvious that there are various causes modifying the amount of the excretion of sulphuric acid.

1. The excretion is augmented by the administration of sulphuric acid, sulphates, and other sulphur compounds whose sulphur becomes oxidised in the body into sulphuric acid.

* Genth (whose investigations on the influence of water-drinking on the metamorphosis of the tissues are deserving of careful study) found that while living on a strictly regulated diet he discharged daily 1252 c. c. of urine containing 2·552 grammes of sulphuric acid; when drinking additionally 1000 c. c. of water the urine rose to 2325 c. c. and the sulphuric acid to 2·751 grammes; when drinking 2000 c. c. of water the urine amounted to 3251 c. c. and the sulphuric acid to 2 985, and when drinking 4000 c. c. of water, the urine rose to 5075 c. c. and the sulphuric acid to 3·274 grammes.

2. During an abundant animal diet the sulphur contained in the protein-bodies of the flesh is probably liberated (or is in a comparatively loose state of combination) as the digestive process advances, and is gradually oxidised in the blood into sulphuric acid.

3. Independently of the introduction of sulphur into the system from without, we may have an augmentation of the sulphuric acid from any internal cause that tends to any great extent to augment the metamorphosis of the tissues.

It is unnecessary to advert to the effect of disease upon the excretion of the sulphates, as Vogel, who has made a large number of observations on this point, declares that he has not been able to arrive at any definite result. It is true that in most febrile diseases we have a very considerable diminution of the sulphates, but this result is doubtless due solely to the ordinary character of the diet in these cases.

Phosphates.

Phosphoric acid is another of the normal constituents of the urine. It occurs partly as the acid phosphate of soda (or, according to Rose, of potash, see p. 135), to which the urine mainly owes its acid reaction, and partly in combination with lime and magnesia.

An adult man excretes daily from 3·2 to 3·8 grammes, or from 50 to 60 grains of phosphoric acid.* The normal range is however a wide one, Breed and Winter finding as their maximum in two cases 6·45, and 3·18 grammes, while Neubauer and Mosler found as their minimum in two cases 1·21 and 1·08 grammes; and even in the same person the quantities may be very different on different days; thus a

* The following include the most trustworthy results regarding the excretion of phosphoric acid :

| | |
|---|---|
| Breed (mean of 4 cases) | 3·7 grammes. |
| Winter, in one case | 3·7 „ |
| „ in a second case | 4·2 „ |
| „ in a third case | 5·2 „ |
| Mosler in one case | 2·4 „ |
| „ in the same case at a subsequent time | 3·7 „ |

man who one day excreted 4·88 on another day excreted only 2·44 grammes (Neubauer), and many similar illustrations might be given. According to Hegar, Gruner and Winter, an adult man excretes daily an average of 0·064 of phosphoric acid for 1000 parts of bodily weight. Winter, Mosler and Vogel agree in the statement that the diurnal excretion of phosphoric acid presents a regular law. The quantity begins to increase in the afternoon (shortly after the principal meal), it reaches its maximum in the evening, falls during the night, and attains its minimum in the forenoon.

The quantity of phosphoric acid in the daily urine is increased by the ingestion of phosphoric acid or of soluble phosphates into the organism; thus Aubert* found that while his normal daily excretion of this acid was 2·8 grammes, it rose after he had swallowed 31 grammes of phosphate of soda to 4·1 grammes.

The amount of the excreted phosphoric acid is much affected by the food; being increased by those foods which contain phosphoric acid or phosphorus-compounds, which by oxygenation in the blood become converted into that acid, and diminishing during prolonged abstinence, without, however, like the chloride of sodium, finally altogether disappearing.† It is more abundant during an animal than during a vegetable diet. (In Professor Haughton's experiments, it was found that the relative daily quantities of phosphoric acid in flesh-fed and vegetarian subjects were 37·1 and 26·7 grains respectively.)

| | |
|---|---|
| Neubauer, in one case | 3·1 grammes. |
| „ in another case | 1·6 „ |
| Genth (mean of two observations) | 3·4 „ |
| Kaupp (mean of two observations) | 3·4 „ |

The above numbers give a general mean of 3·4 grammes.

* Zeitsch f. rat. Med. 1852. New Ser. vol. ii. p. 225.

† Schmidt observed that after prolonged abstinence, a cat excreted daily only one-third of the normal quantity of phosphoric acid. Mosler has made similar observations on man.

Any cause which increases the rapidity with which the metamorphosis of the tissues proceed, augments the excretion of this acid; thus, for instance, after strong bodily exercise or prolonged mental excitement, or after the copious ingestion of water (or watery fluids, such as beer, &c.) we have an augmentation of the phosphoric acid, while after the use of substances which check the rapidity of disintegration, such as coffee and alcohol, we have a diminution of this constituent.

The changes impressed upon the excretion of this acid in disease have been most laboriously studied by Vogel, who has made more than 1000 analyses in reference to this point. His results are, however, not very striking. Even in severe febrile affections there is no very material diminution of the phosphoric acid, probably not more than is due to the altered diet, and again occasionally, even at the very height of an acute disease (pneumonia, for instance), the phosphoric acid may exceed the normal quantity.

We have hitherto been speaking of the collective phosphoric acid that is daily excreted, that, namely, which is combined with soda, together with that comparatively small portion which is combined with the earths. These earthy phosphates — the phosphates of lime and magnesia — now claim some independent notice.

Earthy phosphates.

The earthy phosphates excreted daily by an adult man, amount on an average to 1 gramme.* The quantity, however,

* The following are the most trustworthy of the determinations of the daily quantity of earthy phosphates excreted by an adult male.

| | |
|---|---|
| Lehmann . . . | 1·09 grammes. |
| Beneke . . . . | 1·20 „ |
| Böcker . . . . | 1·48 „ |

Neubauer has made an extended series of observations on this subject, upon four healthy young men with the following results:

1. In the normal state, a young man living on mixed food excretes on an average (taking fifty-two observations) from 0·944 to 1·012 grammes. The ordinary maximum ranged from 1·138 to 1·263 grammes, and on one occasion

is liable to considerable variation, and depends to a great extent upon the nature of the food; thus, for instance, Lehmann found, in experiments upon the effect of different kinds of diet upon his own urine, that while living on his ordinary mixed food, he excreted 1·09, and while living on purely animal food 3·56 grammes. The excess of phosphoric acid which occurs during an animal diet, seems, however, according to Professor Haughton to be distributed in a fixed ratio between the soda and the earths, for he finds that the phosphoric acid in combination with the former, is to that in combination with the latter as 4·1 both in well-fed men and in vegetarians. In the urine of young children and of pregnant women, there is often a great diminution of the phosphate of lime; indeed, after the sixth month of pregnancy, we often fail to detect any indication of its presence.

The determination of the amount of the earthy phosphates in cases of disease is of comparatively little value, because so very large a proportion of them is carried off by the fæces, that the remaining urinary portion affords no trustworthy indication of the rapidity with which metamorphic disintegration is going on.

Iron is usually, although not invariably found in very minute quantities in the urine of perfectly healthy persons. After the medicinal use of ferruginous preparations, iron may sometimes be detected in the fresh urine by the application Iron.

1·554 grammes were excreted. The ordinary minimum was 0·8; once only 0·328 of a gramme was excreted.

2. The phosphate of lime usually ranged from 0·31 to 0·37 of a gramme; the largest and the smallest quantities observed being 0·616 and 0·15 of a gramme.

3. The average quantity of the phosphate of magnesia was 0·64 of a gramme; the observed maximum and minimum were 0·938 and 0·178 of a gramme.

4. About three equivalents of phosphate of magnesia, $2MgO.PO_5$, are excreted for every equivalent of phosphate of lime, $3CaO.PO_5$; and in 100 parts of the collective phosphates there are on an average $67\frac{2}{3}$ of phosphate of magnesia and $33\frac{2}{3}$ of phosphate of lime; a result which is almost identical with that obtained some years previously by Kletzinsky.

of the ordinary tests; generally, however, it is only in the ash that it can be detected. It is a constituent of the urohæmatin described by Harley as the essential normal urine-pigment (see p. 98).

Silica and Fluorine.

Silica, in minute traces, has been detected, in the ash of healthy urine by Berzelius and by Fleitmann; and very minute traces of fluorine have been found in it by G. Wilson and by Nickles.

Ammonia.

(279.) Whether ammonia is a normal constituent of healthy urine, or whether it is merely a product of the decomposition of some of the nitrogenous ingredients of the urine is still a disputed question. Liebig, Scherer, and Lehmann (perhaps the three highest authorities in reference to animal chemistry) deny its presence as a normal constituent, while on the opposite side may be mentioned the names of Heintz, Böcker, Boussingault, De Vry, and Neubauer. The experiments of the last-named chemist, which present no apparent fallacy, show that a healthy adult male excretes daily an average of 0·7234 of a gramme of ammonia, corresponding to 2·2783 grammes of hydrochlorate of ammonia, the form in which, if present, it probably exists in the urine. Lehmann grants that ammonia may occasionally be found in fresh urine, but in these cases he is of opinion that it is formed in the bladder from some change in the extractive matter; and this explanation would give a clue to the interpretation of a result obtained by Neubauer, namely, that very copious water-drinking occasioned an excess of ammonia, for it is well known that watery urine decomposes more rapidly than concentrated urine. We shall in a future page refer to the presence of ammonia in certain forms of morbid urine, in which alkaline fermentation has taken place.

Gases.

(280.) Gases, especially carbonic acid and a little nitrogen, exist in the urine in a state of solution.

Water.

(281.) The quantity of water excreted daily by the kidneys is so variable even under purely physiological conditions, that

it is difficult for us to attempt to fix an average.* It may be more or less modified by any of the following causes; the quantity of water that has been drunk, or that has been absorbed in bathing; the character of the excrements, and the degree of cutaneous excretion, which again is dependent on the temperature and moistness of the atmosphere, upon bodily exercise, &c.

Action of water on the urinary secretion.

From the investigations of Falck, Genth, and others, it appears that after the use of large quantities of water, not only is there more water, but a larger amount of solids, separated by the kidneys. The excess of water is removed from the system in about six hours. The injection of water into the circulation through a vein does not seem to induce a corresponding excess of urine. Shortly after a meal the urine is found to present both an absolute and relative deficiency of water, and an excess of solid constituents.

The free acid of the urine.

(282.) The acid reaction of the urine mainly depends upon the acid phosphates of the alkalies and earths which it contains, but partly also, in some cases, on the presence of free hippuric or lactic acid. To determine the acidity we take a solution of oxalic acid of known strength, and ascertain the relative quantities of a solution (of definite strength) of caustic soda, which are required to perfectly neutralise equal

* The following table, drawn up from memoirs by Scherer and Rummel, shows in certain cases the ratio of the excreted water to 1000 parts of bodily weight.

| | | | | |
|---|---|---|---|---|
| A child aged | 2 years, | 64·33 | parts of water for | 1000 parts of weight. |
| „ | 3 „ | 44·85 | „ | „ |
| „ | 4 „ | 52·50 | „ | „ |
| „ | 5 „ | 40·40 | „ | „ |
| „ | 7 „ | 46·29 | „ | „ |
| A man aged | 18 „ | 42·00 | „ | „ |
| „ | 22 „ | 33·17 | „ | „ |
| „ | 31 „ | 30·40 | „ | „ |
| „ | 38 „ | 24·12 | „ | „ |
| „ | 65 „ | 41·30 | „ | „ |

The last five of these numbers give us for adults a mean of about 34·2 of water for 1000 parts of weight. According to this estimate a man weighing 10 stone excretes daily 4·8 lbs. of water.

volumes of the urine and the oxalic-acid solution. Determined in this way, the total quantity of free acid in the daily urine of a healthy man corresponds in neutralising power to about 2·3 grammes of oxalic acid, the range being from 2 to 4 grammes. It appears from the researches of Winter and Vogel, that in the forenoon the acidity is at its minimum; that during the period of digestion of the principal meal it attains its average; and that in the night it reaches its maximum.*

* There has been so much discussion and difference of opinion regarding the variations in the acidity of the urine, that it seems expedient to notice the principal views that have been propounded on this subject. It was formerly regarded as an unquestioned fact that the normal urine of man was always acid; but in 1849 Dr. Bence Jones (Phil. Trans.), published the view now generally entertained (with some limitation) by physiologists, that the secretions of the stomach and kidneys stand in an inverse relation to one another in regard to their reaction; that when the stomach is empty, the secretion on the surface of its walls is neutral or faintly alkaline, while the urine is strongly acid, that when the stomach contains acid gastric juice (namely, during stomachal digestion), the urine is much less acid or even alkaline, and that, as this acid gastric juice becomes reabsorbed and passes into the blood, the acidity of the urine is restored. Although there is much truth in this view generally, it is not universally true, nor is it always that the urine becomes positively alkaline during digestion. Beneke (Arch. d. Vereins f. wissens. Heilk. vol. i. p. 438) examined his own urine on twenty-three days, and could not discover any connection between its acidity and the digestive process; but states that in a large number of observations on different healthy persons and patients, the urine occasionally, but by no means constantly, exhibited a depressed acidity, or even an alkaline reaction after a meal. Vogel (Anleitung z. Analyse d. Harns.) found that observations made by himself and by his students led to the result given in the text, that the greatest quantity of acid secreted in an hour occurs during the night. Dr. Seller (Edin. Monthly Journ. Jan. 1859) declares that Dr. Bence Jones's law is not "generally applicable in Edinburgh." The latest results are those of Dr. Roberts, of Manchester (Edin. Monthly Journal, March and April, 1860), whose "experiments confirmed in the fullest manner the conclusions of Dr. Bence Jones, that a meal, be it of animal, vegetable, or mixed food, has a powerful and constant effect in lowering the acidity of the urine, frequently even rendering it alkaline." . . . "The effect of dinner," says Dr. Roberts, "was not perceptible until the second hour after the meal. During the next three hours (third, fourth, and fifth hours), the alkaline tide ran in its greatest strength. On the third and fourth hours, the urine was always (with two exceptions), found alkaline when the meal had been of mixed food or animal diet. At the end of the sixth hour the tide had generally turned, and the acid reaction been restored. . . The alkaline urine that was passed after

After the administration of caustic alkalies, their carbonates, or their salts with organic acids, the acidity diminishes, and we often have the urine positively alkaline; while after the administration of acids it is considerably increased.

From a large number of determinations of the acidity, Vogel has arrived at the conclusion that in most diseases, acute as well as chronic, it is diminished; and it is scarcely ever increased except when the mineral acids have been medicinally administered in large doses. It must be recollected that in febrile, and probably other affections, the acid fermentation (see p. 296), ensues very rapidly, giving rise to a large amount of free acid in the urine; hence the acidity should be determined very shortly after the emission.

The close connection between the acidity of the urine and the nature of the food has been shown by Bernard and others. In carnivorous animals the urine is naturally acid; in herbivorous, alkaline; if, however, a carnivorous animal be fed solely on vegetable food, or a herbivorous animal on a flesh diet, the reverse is observed; namely, the urine of the carnivorous animal is alkaline, and that of the herbivorous animal acid. Moreover, in starving herbivorous animals (horses and rabbits), it is found that after a few days their urine is acid,

food owed its reaction to a fixed alkali, and not to ammonia. It did not effervesce with acids. It was rich in earthy and alkaline phosphates; and on these latter, in a basic state, depended apparently its alkaline reaction. As might have been anticipated, the loss of acidity entailed the precipitation of the earthy phosphates; and the urine when passed was frequently turbid. . . The odour of this alkaline urine resembled that of the fresh urine of the horse. It had lost the characteristic urinous odour, and exhaled a strong sweetish aroma, so peculiar as to indicate with certainty the change of reaction without the aid of test paper." Although Dr. Roberts's facts corroborate those of Dr. Bence Jones, his explanation is somewhat different. He maintains that the alkaline tide is concomitant with the absorption of the meal into the blood, rather than with its digestion, and that the passage of the meal into the blood affects the reaction of the urine by temporarily increasing the alkalinity of the blood by the carbonates and basic alkaline phosphates of the food. One of the strongest arguments in favour of this view is the fact, that when food devoid of mineral constituents was used (such as sugar or honey), there was no lowering of the acidity of the urine.

as might, indeed, be expected, for they are then living on their own blood and tissues.*

Incidental constituents.

(283.) We now proceed to the consideration of those substances which, if present in the urine, must be regarded merely as incidental constituents. Putting out of consideration all articles of true food, we may assume that generally only those substances are likely to pass into the urine which are readily soluble in water, which do not form insoluble compounds with any of the tissues of the body, and which are not readily oxidised or decomposed. Thus, the nitrates, chlorates, borates, carbonates, and silicates of the alkalies, and the chlorides, bromides, and iodides of potassium and sodium re-appear unchanged in the urine; while other compounds, as, for instance, the sulphide of potassium, become oxidised, and are eliminated as sulphate of potash, &c. Many substances which form insoluble compounds with the albuminates, as for instance, all the metallic salts, only reappear in the urine when they have been administered in very large quantities.

Various organic bodies appear to experience in their organism the same changes which they may be made to undergo in the laboratory, by means of oxidising agents; and in these cases it is only the products of their oxidation that we can expect to find in the urine: this, for example, is the case with salicin. Others, again, are so perfectly oxidised as to leave only carbonic acid and water as their final products; hence, although they may, in a disintegrated state, pass into the urine, no trace of their existence can be recognised: as is the case with mannite. When, however, very large quantities of substances of this class are taken, a portion passes unchanged into the urine; for example, mannite has under these cir-

* Bernard, moreover, finds that by placing rabbits in an atmosphere of pure oxygen, he can make them excrete for a time an acid urine. He has likewise discovered the singular fact, that on injecting oil into their lungs, their urine rapidly becomes acid.

cumstances been detected by Buchheim and Witte in the urine.

Although as the general rule oxidation is the process to which bodies are exposed in the organism, there are exceptional cases, in which a highly oxidised substance reappears in the urine with a loss of a portion of its oxygen; thus, for instance, indigo-blue appears as reduced indigo; ferridcyanide of potassium (the red prussiate) as the ferrocyanide (the yellow prussiate), &c.

The sulphocyanide and ferrocyanide of potassium, the salts of ammonia and baryta, and most of the organic acids pass unchanged into the urine; tannic acid is, however, converted into gallic acid, and benzoic and cinnamic acids are changed into hippuric acid.* Nitrobenzoic acid is converted into nitrohippuric acid; succinic acid does not reappear in the urine. Uric acid is converted into urea, oxalic acid, carbonic acid, and water. The neutral salts formed by the vegetable acids with alkalies (tartrates, citrates, acetates, &c.) reappear in the urine as corresponding carbonates, and consequently impress upon the urine an alkaline reaction, which usually manifests itself very shortly after their administration.

Oxalic, malic, tartaric, gallic, camphoric, anisic, cuminic, picric, and salicylous acids have been found to pass unchanged into the urine, although in far less quantity than that in which they were administered.

Quinine and urea pass unchanged into the urine, while aniline, theeine, theobromine, allantoine, alloxanthine, amyg-

* Ranke has shown that at a temperature considerably lower than that of the human body, tannic acid has, by the catalytic action of yeast, been converted into gallic acid, and other products. There is strong reason to believe from the researches of Kühne and Hallwachs, that benzoic acid is converted into hippuric acid by combining with glycine in the liver. The combination may possibly be expressed as follows:

1 eq. benzoic acid ($C_{14}H_6O_4$) + 1 eq. glycine ($C_4H_5NO_4$) = 1 eq. hippuric acid ($C_{18}H_9NO_6$) + 2 eq. water (2HO).

dalin, asparagin, phlorrhidzin, and santonin*, are found to yield no indications of their presence. Salicin, if taken in large doses, partly reappears unchanged; in smaller doses it reappears in the form of saligenin, and salicylous, salicylic, and sometimes salicyluric acids.

Most pigments, and many odorous principles, pass unchanged, or only slightly modified, into the urine. Wöhler found in the course of his experiments that the pigments of indigo, madder, gamboge, rhubarb, logwood, red beet-root, and of bilberries, passed into the urine; while those of cochineal, litmus, sap-green, and alkanna could not be detected. To the above list of pigments passing into the urine, that of senna should be added. Both rhubarb and senna communicate a brown tint to the urine, not unlike that produced by blood, but any error from this resemblance may be easily avoided by the addition of a mineral acid, which produces a light yellow colour in the two former, and a darker brown in the latter case.

The odorous principles detected by Wöhler were those of valerian, garlic, asafœtida, castoreum, saffron, and turpentine; he found no traces of camphor or musk.

Rapidity of elimination.

(284.) The rapidity with which substances that have been swallowed reappear in the urine, differs very much. As a general rule, to which, however, there are a good many exceptions, the rapidity is proportional to the solubility of the substance, and to its unchangeability in the system. Iodide of potassium, in a case in which the anterior wall of the bladder was absent, showed itself in the urine in four to ten minutes; usually it does not appear in less than three

* Phlorridzin in a non-nitrogenous compound closely resembling salicin, and obtained from the bark of the root of the apple, pear, &c.; santonin, is a similar compound obtained from *Artemisia contra*. The statement in the text is perhaps rather too strong, as if, after the administration of santonin, the urine be made alkaline either within the system (as by the administration of citrate or tartrate of potash) or externally (as by the addition of ammonia, &c.), it assumes a beautiful red colour.

quarters of an hour, and may even be five hours before it shows itself. After the administration of two or three drachms of bicarbonate of potash, Lehmann observed that the urine of the persons on whom he was experimenting became alkaline in from half an hour to an hour; while after the administration of half an ounce of lactate of soda (calculated as dry) it became alkaline in thirteen minutes. Erichson found that after administering two scruples of ferrocyanide of potassium to a man in whom the anterior wall of the bladder was absent, the salt appeared in the urine in two minutes. He likewise observed that this and other salts passed through the system less rapidly when taken shortly after a meal.

Moreover, the time required for the complete excretion of a substance that passes into the urine varies considerably. Lehmann found that after a dose of two drachms of acetate of soda the alkaline reaction of the urine completely disappeared in ten hours, while after three drachms of bicarbonate of soda the urine remained alkaline for three days. In some persons a dose of ten grains of iodide of potassium leaves no trace in the urine after twenty-four hours; in other persons it may be detected after a space of three days.

Substances which form insoluble compounds with the albuminates are very slowly and gradually eliminated by the urine. Metallic preparations (as of arsenic, lead, copper, mercury, antimony, &c.) may be detected long after their administration in the liver and other parts. We are indebted to Melsens and Hannon for the discovery of the important practical fact, that the elimination of lead and mercury by the kidneys may be much accelerated by the administration of iodide of potassium, which forms in the system soluble iodides of those metals.

Abnormal constituents.

(285.) The incidental constituents of which we have been treating have been introduced into the system from without. We have next to notice those abnormal substances which occur

in the urine in certain forms of disease, and which originate within the body itself.

Albumen. Albumen* is the most important of these abnormal constituents. As its presence may indicate the existence of an intractable disease, while on the other hand it may be of comparatively trifling importance, we must investigate the different conditions which may cause its appearance in the urine.

1. Albuminous urine may be due to some mere local affection of a limited portion of the uropoietic tract. Thus any lesion occasioning the presence of blood or pus in the urine renders it albuminous; in cases of this nature a sediment will occur, and its microscopic examination will reveal the nature of the foreign admixture. The reflux of spermatic or prostatic fluid into the bladder may possibly have a similar effect.

2. The urine may become albuminous in certain forms of renal irritation and congestion, in which the action of the capillaries is so far altered as to admit of the permeation of albumen through their walls. Thus we sometimes find the urine albuminous after the administration of cantharides and other highly stimulating diuretics. A similar condition may also be induced mechanically by tying the renal veins, or the aorta just beyond the point at which the renal arteries are given off; by the injection of large quantities of water into the blood; and in short by anything that increases the pressure of the blood in the capillaries of the kidneys. In this way certain diseases of the liver, heart, and lungs may cause albuminous urine.

3. Independently of any renal affections, it is more than probable that certain conditions of the blood, due to altered metamorphosis of the tissues, may occasion the escape of albumen through the capillary walls into the urine. Thus,

* The remarks upon the presence of albumen are taken almost *verbatim* from Vogel's Semiotik des menschlichen Urines: a work from which I have borrowed freely in this chapter.

for instance, when the blood-serum is very poor in albumen and rich in water we very frequently find some of the albumen, escaping into the urine. Again, it has been ascertained (in experiments on animals), that the injection of albuminous solutions into the blood often (but not invariably) renders the urine albuminous, and the discrepancy in the results has led to the hypothesis that some modifications of albumen may pass more readily through the walls of the renal capillaries than others; and that such modifications can be produced in the albumen of the blood by certain forms of disease. Whether these modified conditions of the blood are accompanied by a perceptible change in the tissue of the kidneys (hyperæmia, and distention of the capillaries) is uncertain; but even if it occur, it is only of a temporary character; and hence, from the mere existence of albuminuria, unsupported by other evidence, we must not infer the necessary existence of those organic changes in the kidney which are known as Bright's disease. Putting out of consideration other symptoms, we cannot conclude from the urine that Bright's disease is present, unless (1) albumen has been long and constantly present, and (2) unless fibrinous casts are simultaneously present in the urine (see pp. 372-4).

The only diseases in which albumen is almost invariably present in the urine, are Bright's disease and the other diseases with which uræmia is associated, such as the dropsy occurring after scarlatina, cholera, and partial suppression of urine. There are, on the other hand, few acute diseases in which it is not sometimes found.*

Albuminous urine is occasionally observed in persons who are apparently quite healthy.

* Finger (of Prague), examined the urine of 600 patients for albumen. In 88 cases of typhus it was found 29 times, in 46 of puerperal fever, 32 times; in 33 of pneumonia, 15 times; it was of more rare occurrence in intermittent fever, pleurisy, peritonitis, and mucous diarrhœa, and was not found once in 18 cases of acute rheumatism.

Fibrin. Fibrin is stated occasionally to occur, independently of blood-corpuscles, in the urine. In these cases the intercellular fluid of the blood must permeate the walls of the capillaries. The fibrin seems to remain fluid till after the urine is discharged, when it separates in clots, granules, or stringy masses. The chylous or milky urine, described by Rayer, Bence Jones, and others, contains fibrin in addition to other abnormal constituents.

The occurrence of fibrinous casts or tubes in the urine will be noticed in the remarks on urinary sediments.

Casein. Casein has never been detected with certainty in the urine.

Other protein-bodies. Protein-bodies, differing from albumen, fibrin, and casein, occasionally occur in the urine. Through the kindness of my friend, the late Dr. Macintyre, I had the opportunity of examining a very remarkable variety of urine passed by a patient with mollities ossium. It contained a protein-body, as was evidenced by the reactions of acetic acid, ferrocyanide of potassium, and strong hydrochloric acid; but this body differed from the ordinary substances of this class in being soluble in boiling water, and in the nitric-acid deposit being soluble on warming, and being again thrown down on cooling.*

Fat. Fat does not occur, except in the slightest trace, in normal human urine. There are, however, some forms of disease in which it occurs in appreciable quantity; as, for example (and especially), in Bright's disease†, in rhachitis, hepatitis, cirrhosis of the liver, and chronic insanity. According to Lehmann, fat-globules are often found in the urine of persons who are becoming rapidly emaciated from any disease. The same observer also notices that in the milky or chylous urine, previously mentioned, the turbidity is not mainly due to

* The chemical characters of this substance were described by Dr. Bence Jones in the Philosophical Transactions for 1847.

† Kletzinsky found the following quantities of fat in 1000 parts of urine in cases of Bright's disease, 0·24, 0·26, 0·28, 0·35, 0·37, 0·48, 1·27. Beale in one case found a much larger quantity.

fat-globules (as was generally believed), but to pus-corpuscles, which, however, contain a considerable amount of fat. Cholesterin has been detected by Beale* on several occasions in the urine in Bright's disease.

While there can be no doubt that fatty degeneration of the kidneys is the most common cause of an excess of fat in the urine, it is not improbable that wherever there is, from any cause, an excess of fat in the blood, a portion may be eliminated by the kidneys.

Sugar.

It has been already stated in page 89 that sugar does not occur in healthy urine, and we have there briefly noticed the conditions under which it appears in that fluid.†

* Archives of Medicine, vol. i. p. 8. A notice of the only other cases on record may be found in my Translation of Simon's Animal Chemistry, vol. ii. pp. 313 and 333.

† Brücke has recently attempted to prove that sugar is a normal constituent of human urine. The following is his method of procedure. Freshly passed urine was treated with four times its volume of absolute alcohol, and filtered; to this clear filtered fluid an alcoholic solution of potash was added, and after six, eight, or ten hours there was observed a crystalline efflorescence at the bottom and on the walls of the vessel, together with a slight amorphous precipitate. This deposit, when collected and dissolved in water, gave, on being boiled with sulphate of copper and potash, a beautiful red precipitate of suboxide of copper. That it is not, however, sugar, as Brücke supposes, which occasions this reduction of the oxide of copper, seems obvious for the following reasons. (1.) He found that the extent of the reduction varied in a direct ratio with the amount of the crystalline efflorescence; but potash-sugar does not separate from an alcoholic fluid in a crystalline form (see p. 86). (2.) Again, to obtain the reduction at once, he had to employ a boiling heat, whereas the presence of sugar manifests itself at a temperature of 160° or less (see my remarks on the precautions to be attended to in the application of Trommer's test in p. 86); and while at an ordinary temperature sugar exhibits its reducing powers in from two to twelve hours, in Brücke's cases no separation of the suboxide was perceptible, even after the mixture had stood for twenty-four or forty-eight hours; although after a longer period a very trifling scarcely visible precipitate was found. (3.) If we slightly acidify the watery solution of the efflorescence with hydrochloric acid, minute, colourless crystals of uric acid are formed in a few hours, and after their removal the fluid altogether loses its power of reducing oxide of copper.

The main factor, then, in the reduction in these experiments is clearly uric acid; and Lehmann, who has carefully repeated Brücke's observations, suggests that hypoxanthine, and some other substances which sometimes occur in traces in the urine (such as taurylic acid, and aldehyde), may co-operate with the uric acid in this action.

If the urine constantly, and for a considerable time, contain an appreciable quantity of sugar, we may be tolerably certain (independently of other signs, such as an increased quantity of urine, high specific gravity, &c.) that the case is one of diabetes mellitus.

If, on the other hand, the urine only contains traces of sugar, or if the presence of the sugar is only temporary or intermittent, we should act very rashly in assuming that the case was necessarily one of diabetes mellitus. In such cases as these, the presence of sugar may be due to the excessive use of saccharine or farinaceous food, to an abnormal condition of the medulla oblongata, to a diminution of the respiratory activity and of the consequent supply of oxygen to the system, to an excessive production of sugar in the liver, to a sudden stoppage of the secretion of milk *, or to a diminution of the alkalies of the blood.

The effect of sugar, saccharine fruits, &c. in increasing the quantity of the sugar in the urine of diabetic patients, has been long known. Recent investigations have shown that coffee, wine, beer, and organic acids have a similar action, while the accession of a febrile attack temporarily diminishes the quantity of sugar.

Inosite.

Inosite has been found by Cloetta in the urine of a patient with Bright's disease, who was being treated with drastic purgatives; and by Vohl, in a diabetic patient in whose urine it partially replaced the ordinary sugar (glycose.)

Leucine and Tyrosine.

Leucine and tyrosine have been found in a few instances in the urine in cases of typhus, measles, and acute yellow atrophy of the liver: leucine has also been found in alkaline albu-

* The statement of M. Blot (see note to p. 91), that sugar is usually present in the urine during pregnancy and the puerperal state, and often during lactation, has not been confirmed. I am indebted to Mr. Jardine Murray, late house-surgeon to the Edinburgh Maternity Hospital, for a very careful examination of the urine in thirteen cases, in reference to this point, the fluid being obtained in most cases a very few hours before delivery. In no case could a trace of sugar be detected; but in seven of the cases the urine was slightly albuminous.

minous urine, passed by an epileptic patient with disease of the spinal cord. In some of these cases the leucine was partially decomposed into valerianate of ammonia. (see p. 31).

Bile-pigment.

Bile-pigment, probably an admixture of cholepyrrhin and biliverdin, is found in the urine in almost all cases of icterus. According to Vogel, the biliverdin is usually the preponderating pigment, and sometimes we find biliverdin alone. Since cholepyrrhin is probably the original pigment and biliverdin only a derivative from it (see p. 96), we are led to infer that in icterus the greater part of the bile-pigment undergoes a change, either during its resorption, or subsequently in the blood, or finally in its passage into the urine.

Biliary acids.

The presence of biliary acids in morbid urine is by no means so rare as has generally been supposed. Until very lately, it has been believed that they seldom occur in the urine; but this may probably be, as Vogel suggests, because they have been seldom sought for. Pettenkofer, Enderlin, and Lehmann, have detected them, sometimes unaccompanied by bile-pigment, in the urine in cases of pneumonia; and so far as I know this was the only disease in which they had been discovered, till Kühne recently proved by very careful experiments, both on jaundiced patients and on dogs that were artificially jaundiced by ligaturing the ductus communis, that cholic acid (not however in a conjugated form as glycocholic or taurocholic acid) is usually present in bilious urine.

Ammonia.

We have already alluded to the question as to whether ammonia is a normal constituent of the urine (see p. 322). It is universally known that ammoniacal salts occur in morbid alkaline urine; but they are also occasionally found in acid urine in cases of typhus, measles, and scarlatina. Ammonia is almost always present in alkaline urine, for the alkaline reaction either depends directly on ammonia produced (as in vesical catarrh) from decomposition of the urea, or is due to the passage of alkaline carbonates into the urine,

which rapidly induce a decomposition of the urea; in the latter way we can explain the invariable occurrence of a little ammonia in the normally alkaline urine of herbivorous animals, and in the urine of man after the administration of alkaline carbonates, citrates, tartrates, &c.

There is no satisfactory evidence that nitric acid ever occurs in the urine, unless when it had been previously administered.

Variations in the quantity of the urine.

(286.) The remarks which have been already made (see p. 323) on the quantity of water excreted daily by the kidneys apply almost equally to the urine itself. The quantity may be determined either by weight or by fluid measure; in this country we almost always calculate it by fluid ounces, on the continent it is most commonly reckoned by weight (grammes), but sometimes by cubic centimetres (thirty of which nearly equal one fluid ounce). The most careful and prolonged set of experiments made on this subject are those of Dr. Thudichum. They were made upon two individuals, (A) a man aged 28 years, and weighing 11 stone; and (B) a man aged 28 years, and about 5 pounds heavier. Observations made on A for 76 days gave as an average 69 ounces, the maximum being 100 and the minimum being 36 ounces; while similar observations made on B for 57 days gave as the average 61 ounces, the maximum being 92 ounces and the minimum 35 ounces. Other determinations by Bischoff and Vogel are lower. From 40 to 70 ounces may be said to be the normal range. Measuring the urine in reference to the weight of the individual, (which is undoubtedly the fairest mode,) it has been found that for 1000 parts by weight an adult male excretes daily 25·9 parts according to Winter, 24·24 parts according to Vogel, and 20·26 parts according to Kaupp; while, according to Scherer, a child excretes 47 parts of urine for 1000 of weight. It appears from hourly observations made by various observers, that the excretion is most abundant after dinner, reaches its minimum during the night, and rises again in the forenoon. Cold fresh-water

bathing often increases it considerably for a short time, and so, to a much less extent, does sea-bathing. The temperature of the atmosphere also affects the excretion, most urine being voided at low temperatures when the action of the skin is comparatively inert. We possess little or no certain knowledge regarding the direct action of medicinal agents on the excretion of urine.*

In disease the quantity of urine often deviates beyond the normal range.

1. In almost all acute febrile affections the quantity of urine is diminished, and does not begin to rise till the disorder begins to abate. The observance of the daily urine thus affords an important prognostic indication. It is found that it is almost solely the water that is diminished in these cases, the daily solid constituents being comparatively unaffected.

2. Towards the fatal termination of most diseases, both acute and chronic, the quantity of urine often sinks considerably below the normal standard.

3. In dropsies we usually have a great diminution of the urine.

4. The only diseases in which there is an excessive excretion of urine are Diabetes mellitus, and D. insipidus.

Variations in the amount of solid constituents.

(287.) It appears from numerous observations that in adults the daily amount of the solid constituents of the urine may vary from 35 to 80 grammes, according to the quantity and nature of the food. The ingestion of much fluid augments the solid constituents. During the night less solid constituents are passed than in the same number of hours during the day. The main function of the kidneys being to excrete nitrogenous matters and soluble salts, it is almost *à priori* obvious that a highly nitrogenised (animal) diet and

* Hammond has carefully examined the action of digitalis, broom, squills, and colchicum on the urinary secretion ; and finds that while colchicum materially increases both the organic and the inorganic solids, the other drugs actually diminish the excretion of organic matters. They all increase the quantity of water. (Quoted in Journ. de Physiol. 1860, vol. iii. p. 227.)

any circumstances that accelerate metamorphic action of the tissues must increase the solid constituents of the urine, as indeed has been rigorously demonstrated by the observations of Lehmann, Bischoff, Rummel, Hammond, and others. When the metamorphic action is checked, as is the case in many forms of disease, the solid matters are diminished. When the blood is poorer than natural in albuminates and richer in salts, the normal solid constituents are considerably diminished, as we see in Bright's disease (after the removal of the albumen from the urine), and in cases in which saline solutions have been injected into the veins of animals. In diabetes we always have an excessive amount of solid constituents; and the same is often the case in Bright's disease, if we include the albumen.

Daily quantity of salts.

The daily quantity of the mineral constituents is liable to great variations; it may range from 7 to 23 grammes, the average being about 15 grammes, or nearly half an ounce.

It is unnecessary to refer to the conditions which modify the amount of the collective salts, as we should merely have to recapitulate what has been already stated regarding the individual salts.

(288.) We shall next consider the influence of certain physiological relations, such as sex, age, food, &c., upon the urinary secretion.

Influence of sex.

It has been generally stated that the urine of women contains more water and less urea and salts than that of man; it is doubtless true that the daily excretion of urea and salts is less in women than in men generally; but this difference is due, not to anything special in the sex, but to the fact that in man, owing to his greater weight and more active habits, there is usually a greater disintegration of tissue than in woman. The urine during pregnancy is distinguished by its small amount of solid constituents, and by its especial poverty in phosphate of lime (which is required for the fœtal bones, &c.). Becquerel never found it to possess a higher specific

gravity than 1·011. According to Lubanski and Mosler, the urine during pregnancy is deficient in free acid, the reaction being often neutral or alkaline; Lehmann, however, found it always acid in healthy women. In consequence of its watery character, alkaline fermentation sets up in it earlier than in ordinary urine; and a glistening scum or membrane is usually formed in the course of a day or two upon its surface, to which the term *kyesteine* has been applied. This membrane, which was at one time regarded as a certain evidence of pregnancy (and which unquestionably is generally present in the urine during pregnancy, although it is not exclusively connected with that condition), is merely a conglomerated admixture of triple phosphate crystals (phosphate of ammonia and magnesia), and minute fungoid and confervoid growths. It is not unfrequently formed on the surface of the urine of chlorotic and anæmic non-pregnant women.

Of age.

The urine at different periods of life presents variations in its character which correspond with the variations occurring at different epochs in the general metamorphosis of the tissues. It appear from the researches of Scherer, Bischoff, and Rummell, that while men in the prime of life excrete positively the largest amount of urinary constituents, the largest quantity as compared with the weight is yielded by children (in the ratio of nearly two to one). Except that young children pass relatively much less phosphate of lime, and possibly rather more hippuric acid, their urine does not materially differ from that of adults.

Of the digestive process.

The influence of the digestive process upon most of the individual constituents has been already noticed; and although the same remark applies to a great extent to the influence of different kinds of diet, the subject is one of such importance that we shall notice it here more fully.

Of different kinds of food.

The most important investigations on the effects of different kinds of diet on the urine are those of Lehmann and Hammond.

In a prolonged series of experiments, to which we have already referred (see p. 43), Lehmann attempted to ascertain the influence which varieties of diet (animal, vegetable, and non-nitrogenous) exert on the character of the urine generally, and on its special quantitative relations. Having first determined the composition of the daily urine during his ordinary mixed diet, he analysed for twelve days the urine while he lived on a purely animal diet (chiefly of eggs), and for twelve days while living on a purely vegetable diet; and he further made two analyses, while living on a perfectly non-nitrogenous diet (fat, milk-sugar, and starch).

The following table expresses the mean results (in grammes): —

| | Solid Constituents. | Urea. | Uric Acid. | Extractive Matters and Salts. |
|---|---|---|---|---|
| On a mixed diet | 67·82 | 32·498 | 1·183 | 12·746 |
| On an animal diet | 87·44 | 53·198 | 1·478 | 7·312 |
| On a vegetable diet | 59·24 | 22·481 | 1·021 | 19·168 |
| On a non-nitrogenous diet | 41·68 | 15·408 | 0·735 | 17·130 |

From these researches he draws the following conclusions: —

(1.) The solid constituents are much increased by animal food, while they are considerably decreased by a vegetable diet, and still more so by a non-nitrogenous one.

(2.) The urea is similarly affected.

(3.) The uric acid is not essentially affected by the nature of the food.

(4.) The sulphates and phosphates which are discharged correspond very nearly in quantity with the nitrogenous matters which have been taken; after the almost exclusive use of protein-compounds, the quantity of these salts in the urine is considerably increased.

(5.) Hence it follows that the other organic constituents of the urine, that is to say the extractive matters, must be very much diminished during an animal diet, and these investigations show that the use of vegetable food causes a positive augmentation of such substances.

(6.) After the use of purely animal food the physical properties of the urine precisely resemble those of this secretion in the carnivora; that is to say, the secretion is of a very light amber-yellow colour, has a strong acid reaction, and contains little or no lactic acid, and no hippuric acid. On the other hand, after a course of vegetable diet, a very great portion of the free acid disappears; the urine contains a large amount of dark-coloured extractive matter, and hence is of a brownish-red tint; it is also somewhat turbid from the separation of earthy phosphates, or rapidly becomes so on boiling, and almost always contains alkaline lactates with oxalate of lime.

Dr. Hammond first ascertained the normal composition of his urine, while living on his ordinary diet, by analysing it for five successive days; he then lived for ten days solely on albumen and water, and analysed his urine each day; after an interval of a month he lived for ten days on cooked starch and water, analysing the urine each day; twenty-five days after the termination of this set of experiments he commenced living on gum and water, which, much to his regret, he was obliged to discontinue, "owing to the debility and great derangement of health produced" at the end of the fourth day, the urine being analysed on each of these days.

The following table gives his mean results expressed in troy grains: —

| | Ordinary Diet. | Albumen. | Starch. | Gum. |
|---|---|---|---|---|
| Solid constituents | 1097·58 | 988·87 | 516·98 | 440·50 |
| Urea | 694·63 | 715·19 | 215·35 | 297·13 |
| Uric acid | 11·67 | 20·76 | 7·53 | 8·81 |
| Chlorine | 138·13 | 8·86 | 16·71 | 19·21 |
| Sulphuric acid | 45·18 | 16·92 | 9·73 | 11·12 |
| Phosphoric acid | 55·85 | 22·04 | 13·66 | 12·28 |
| Residue | 194·37 | 215·19 | 252·86 | 67·16 |

The high numbers for urea, &c., during his ordinary diet are explained by the facts that Dr. Hammond's normal weight

is between 14 and 15 stone, and that he takes animal food three times daily.

As these experiments will again claim our notice in the chapter on "Nutrition," it will be sufficient to mention that the albumen was obtained from the serum of bullocks' blood by boiling it, and was consequently ingested in the coagulated form. The water was either distilled, or obtained by melting snow, and nothing was taken during the 10 days of the albumen-experiment but washed coagulated albumen and water. On the 7th day albumen appeared in the urine, and continued, in increasing quantity, to the close of the experiment. Amongst the other points most worthy of notice in this experiment, may be mentioned — (1.) The fact that the urea obviously varied in a direct ratio with the amount of ingested albumen till the health got considerably disturbed.

Thus on the —

| | | Grains. | | Grains. |
|---|---|---|---|---|
| 5th day | the ingested albumen was | 6,680 | and the urea | 721 |
| 2nd | „ „ | 8,653 | „ „ | 922 |
| 1st | „ „ | 8,729 | „ „ | 812 |
| 3rd | „ „ | 11,285 | „ „ | 1,162 |
| 4th | „ „ | 12,725 | „ „ | 1,251 |

(2.) There is no definite ratio between the uric acid and either the urea or the ingested albumen. (3.) No chlorides being taken during this experiment, there was a regular and steady daily fall in the excreted chlorine, it standing during the 10 days as follows: — 30·6, 21·6, 10·5, 5·4, 5·0, 4·2, 3·6, 3·4, 2·4, and 2·1 grains. In the starch-experiment sugar was found in the urine on the 5th day, continued in increasing quantity to the 10th and last day of the exclusive starch-and-water diet, and remained in the urine five days after the close of the experiment: the urine remained acid during the starch-diet. The urea fell tolerably regularly from the beginning to the end of the experiment, being 422 grains on the

1st day, 204 on the 4th, 157 on the 7th, and 122 on the 10th day, and was unaffected by the quantity of ingested starch. The uric acid presented no definite law, but was present in far less quantity than during the albuminous diet. In that case the maximum, mean, and minimum were 29·2, 20·8, and 11·3 grains; while on the starch diet they were 9·5, 7·5, and 5·2 grains. The chlorine diminished regularly, as in the former experiment; and in this case the sulphuric and phosphoric acids similarly diminished from 30·4 and 27·2 to 2·3 and 5·3 grains, while in the former case they were slightly modified by the amount of albumen, although on the whole they sunk with tolerable continuity, the sulphuric acid from 28·7 to 8·4, and the phosphoric acid from 36·2 to 9·2 grains.

Dr. Hammond's observations confirm the generally accepted view that gum is incapable of assimilation; hence in the last set of observations the urinary constituents must have been solely derived from the pre-existing tissues of the body.

Urine in disease.

(289.) We now proceed to notice the changes which the urine undergoes in certain general forms of disease, which express upon it definite and well marked characteristics.

Febrile urine.

The urine in fever, that is to say, in that group of symptoms which accompany almost all acute diseases, presents distinct peculiarities. Febrile urine is usually more deeply coloured than usual (being of a reddish tint), and has a stronger odour, a higher specific gravity, and a more decided acid reaction than normal urine. As long as the febrile symptoms continue, less than the normal quantity of urine is generally secreted by the kidneys, and the urine is concentrated, because there is a greater relative diminution of water than of solid constituents. The constant characters of such urine are the diminution, both relative and absolute, of the inorganic salts, and especially of the chloride of sodium, and the augmentation of the uric acid and urates. Even when febrile urine does not deposit urates, it is always richer in

uric acid than other urine. The urea is increased in some febrile urines (see p. 45), and probably diminished in others. The extractive matter is usually increased, and lactic acid is often present.

Anæmic urine.

In contrast to febrile urine, Becquerel has distinguished an anæmic urine, which is connected with a deficiency or poverty of the blood, and occurs in various forms of debility. Anæmic urine is pale and watery; it has only a slight acid reaction, and readily becomes alkaline; the urea and uric acid are much diminished, and there is a decrease, to a less degree, in the salts, while the extractive matters differ only slightly from the normal average.

Difficulties in the investigation of the urine in disease.

We shall not attempt to describe the modifications of the urine in individual diseases, for even in health, and still more in disease, this fluid is of so variable a nature, that it is often impossible to determine whether the alterations noticed in its condition actually arise from a morbid process, or only from incidental influences. "If," says Lehmann, "we carefully observe the changes which often occur in the urine in the course of the same day, not merely in typhus or any acute exanthema, but also in inflammations which are running their ordinary course, we see that the urine is much more regulated by the transient condition of the organism, external influences, and temporary symptoms, than by the nature of the morbid process. Thus, the albumen in the urine in Bright's disease is considerably diminished, and may even almost disappear, if the chronic form of this disease is associated with an affection giving rise to inflammatory fever. The urine which is so characteristic of this form of disease, loses almost all its distinctive properties, and assumes, both in a qualitative and quantitative point of view, the character of inflammatory febrile urine. It appears therefore to be more rational to limit our examination of the composition of the urine to certain morbid conditions and individual groups of symptoms, and to compare together the various analytical results thus

obtained, than to attempt to extend similar observations to different forms of disease."

Again, every one who has paid any attention to the chemical composition of the urine, must have observed that such substances as albumen, oxalate of lime, lactic acid, &c., are not characteristic of specific diseases, or even of specific groups of disease, but merely of certain processes or symptoms accompanying disease: and if the more abnormal substances which are occasionally present, such as red, green, blue or black pigments, inosite, cystine, leucine, tyrosine, &c., do indicate the existence of special forms of disease, we have hitherto been unable to trace the connection.

Urine of animals.

(290.) Many analyses have been made of the urinary secretion of the lower animals. It is sufficient here to indicate the most important of the general results which have been obtained.

The urine of the pig, which may be regarded as the type of the omnivora (but whose food when domesticated is chiefly vegetable), is clear, almost devoid of odour, distinctly alkaline, effervesces on the addition of acids, and becomes turbid on boiling from the conversion of the alkaline bicarbonates into simple carbonates. It contains neither uric nor hippuric acid, no salts of ammonia, and mere traces of phosphates. Sulphates and alkaline chlorides are tolerably abundant, and alkaline lactates are apparently contained in it. Its solid constituents range, according to Boussingault and Von Bibra (who have independently analysed this fluid), from 1·804 to 2·086% of which from 0·29 to 0·49% are urea.

The urine of the carnivora approaches much more closely to the human type. When fresh, it is clear, of a light yellow colour, and has a disagreeable odour, a nauseous bitter taste, and an acid reaction. It contains much urea, little pigment, and little or no uric acid. (In dogs * the uric acid seems to be

* A thorough series of analyses of the urine of the dog under different conditions of diet, has been made by Voit. (See Bischoff u. Voit, Die Gesetze der Ernahrung des Fleischfressers, 1860, pp. 267—288.)

partly replaced by an acid whose probable formula is $C_{16}HNO_5$, and which we may name cynuric acid.) By feeding carnivorous animals on vegetables we can render their urine turbid, alkaline, and generally like that of the herbivora.

The urine of herbivorous animals is yellow, turbid, of an unpleasant odour, and alkaline. In addition to urea, it contains hippuric (but no uric) acid, lactates of the alkalies, carbonates of the alkalies (chiefly potash) and earths, oxalate of lime, and a very small quantity of phosphates. By placing herbivorous animals on a purely animal diet, we can make their urine resemble that of the carnivora. Thus, the urine of the calf while living solely on milk is clear and acid, and in addition to urea, contains uric (but no hippuric) acid, creatinine, and a considerable quantity of allantoine (see p. 49), a large amount of phosphate of magnesia and potash-salts, but very little of the alkaline phosphates, sulphates, or soda-salts.

The urine of birds, which usually forms a white outer coating to the solid excrements, consists essentially of the urates of ammonia and lime, together with phosphates, sulphates, and chlorides.

The urine of frogs is fluid, and contains urea, chloride of sodium, and a little phosphate of lime.

The urine of serpents, which is often passed independently of the solid excrement, is at first pulpy, but soon becomes firm and dry. It consists mainly of urates of the alkalies, a little urea, and earthy phosphates. (Prout found more than 90% of uric acid in the urine of the boa constrictor.)

The urine of tortoises, when they have been kept for some time without food, is a very pale yellowish green fluid, with a well-marked acid reaction, which on cooling deposits a sediment, which redissolves on the application of warmth; if they have been recently fed, their urine is neutral, or faintly alkaline and less clear, and deposits a sediment which is only partially soluble in boiling water. The main ingredients of their urine are urea, urates of soda, ammonia and lime,

hippuric acid, a little fat, phosphates, sulphates, and chlorides.

The urine of several Saurians has been examined. In that of *Lacerta agilis* Scholz found 94% of uric acid, 2% of ammonia, 3·33% of phosphate of lime, and 0·67% of sand. Prout analysed the urine of the chameleon and iguana, and obtained similar results; and the urine of the crocodile has been separately examined by Drs. John Davy and W. Moore: it contains a large quantity of uric acid and urates, but no urea; in Dr. Moore's case albumen was also present, but this was doubtless abnormal.

In the Invertebrata we often find urinary constituents (uric acid and urates) mixed with the excrements, and we not unfrequently meet with uric-acid crystals in examining certain glandular structures, which we must consequently regard as acting the part of kidneys, as for instance in the Malpighian vessels of insects, spiders, and myriapods, in the glandular venous appendages of the cephalapods, in Cuvier's mucus-gland in the gasteropods, and in Bojanus's organ * in the lamellibranchiate mollusks.

Sketch of analysis of urine.

(291.) Although it does not enter into the scope of the present volume to describe analytical details, yet a general knowledge of the chemistry of the urine is so important to the medical practitioner, that I shall so far deviate from my prescribed course, as to indicate the general steps to be pursued for the detection of the ordinary normal and abnormal ingredients of that fluid.

1. After having noted the specific gravity, we ascertain the reaction of the urine by test-paper.

(*a.*) If the urine is acid and contains no sediment we proceed according to 2.

(*b.*) If the urine is acid and sedimentary, we allow the

* It seems well established by the independent chemical investigations of Garner, Von Hessling, Von Babo, Will, and Von Gorup-Besanez, that this is a urinary organ. Schlossberger, however, failed in detecting any uric acid in a large brown concretion obtained from this organ in *Pinna nobilis*.

sediment to deposit itself, decant off the urine (or filter if requisite) and proceed according to 2. The sediment must be examined microscopically according to the rules given in pp. 357 and 375.

(*c.*) If the urine is neutral or alkaline, it generally contains a sediment which must be examined with the microscope, while we proceed with the decanted or filtered fluid according to 2.

2. We boil a small quantity of the urine in a test-tube, having previously acidified it with acetic acid if its own reaction was not acid. If a coagulum is formed which does not dissolve on the addition of a drop of nitric acid, it must consist of albumen. In this case we take a larger quantity of urine, about three ounces, remove the albumen by boiling, filter, and treat the filtrate according to 3.

The coagulum may be

(*a.*) *White*, in which case it consists of pure albumen.

(*b.*) *Greenish*, in which case bile-pigment is probably present; or,

(*c.*) *Brownish-red*, in which case blood is probably present, and the sediment should be carefully examined for blood-discs.

3. About two ounces of clear acid or acidified urine, freed from any sediment or from albumen, must be evaporated in a water-bath to the consistence of a thick syrup, and extracted with alcohol. We filter the solution thus obtained, return the insoluble residue, after washing it with alcohol, to the evaporating basin, and test both the solution and the residue as follows:—

(*a.*) One-third of the alcoholic solution is evaporated to a very thick syrup, and tested by nitric or oxalic acid for urea (see p. 40).

(*b.*) Two-thirds are treated with oxalic acid and are evaporated almost to dryness. The residue is then extracted with ether, to which about one-sixth of alcohol has been added. If we evaporate the ethereal solution to dryness, dissolve the residue in a few drops of water, filter, and allow the solution

to evaporate spontaneously in a watch-glass, we shall obtain crystals of hippuric acid, if any is present. If any fat is present it will be found on the filter.

(*c.*) The residue insoluble in alcohol is treated with dilute hydrochloric acid and filtered.

(*aa.*) The filtrate contains the earthy phosphates and other salts; the former may be precipitated by neutralisation with ammonia.

(*bb.*) The residue on the filter contains uric acid and mucus. These may be separated by washing them off the filter into a small test-tube, adding two or three drops of a soda-solution, warming, and filtering.

(*a.*) The substance that still remains undissolved is mucus.

(*β.*) The filtrate contains urate of soda, which, on the addition of hydrochloric acid, yields crystals of uric acid, whose character may be further tested by the microscope and by the murexide reaction.

4. If the urine is of a dark brown or greenish tint, if it froths much when shaken, and if it communicates a yellow or green tint to a bit of filtering paper moistened in it, we must suspect the presence of bile, which may be further tested for as follows: —

(*a.*) We place some of the suspected urine in a conical glass, and quietly drop into it some fuming nitric acid. If we observe that the fluid assumes various colours, becoming green, blue, violet, red, and finally yellow, we may be certain that these changes are due to the oxidation of the cholepyrrhin or brown-colouring matter of the bile.

(*b.*) A second portion is precipitated with acetate of lead; the precipitate is collected on a filter, washed, dried, and treated with alcohol, to which a few drops of sulphuric acid have been added. If the fluid, after filtration, have a green tint, biliverdin, or the green colouring matter of the bile, is present.

(*c.*) We take a third portion, about half an ounce, evaporate it in the water-bath to dryness, extract it with alcohol, evaporate the alcoholic solution, dissolve the residue in water, add three or four drops of syrup (1 part of sugar to 4 of water), and then a little strong sulphuric acid, taking care that the temperature does not rise much above 120°. If the fluid, after becoming turbid, assumes a red or purple tint, we have evidence of the presence of the resinous acids of the bile.

5. If from the high specific gravity or for any other reason we suspect the presence of sugar, we proceed as follows: —

(*a.*) We apply Trommer's test of sulphate of copper and solution of potash (see p. 85); and if the quantity of sugar is very small, and the reactions doubtful, we must follow the rules laid down in p. 86.

(*b.*) Or we boil a little urine in a test tube with an equal quantity of solution of potash, when if sugar is present a sherry brown colour is produced. This is, however, not so certain a test as Trommer's.*

6. We treat half an ounce of urine with half its volume (or more) of strong hydrochloric acid. If a dark colour is developed, and after a time a blue powder deposited, we have evidence of the presence of indigo.

7. To test for the presence of the inorganic ingredients, we may evaporate a portion of the urine (an ounce or less will suffice) to dryness, mix it with a little spongy platinum †, and heat it till all the carbonaceous matter is burnt off. We boil the residue in water, filter, and proceed as follows: —

(*a.*) We acidify one portion of the filtrate with hydrochloric acid, and add chloride of barium. A fine white precipitate indicates the presence of sulphuric acid. (Sulphate of baryta.)

* We must not, however, forget that uric acid possesses a slight power of reducing oxide of copper. See p. 333.

† The spongy platinum is added to ensure free and abundant access of air to the interior of the heated mass.

(*b.*) We acidify another portion with nitric acid, and add nitrate of silver; a white curdy precipitate indicates the presence of chlorine. (Chloride of silver.)

(*c.*) We treat a third portion with acetate of soda, acetic acid, and a drop of a solution of perchloride of iron; a yellowish white gelatinous precipitate indicates the presence of phosphoric acid.* (Phosphate of iron.)

(*d.*) We evaporate the remainder of the watery solution to dryness, and heat a portion of the saline mass on a piece of platinum wire in the inner flame of the blow-pipe. A yellow coloration of the apex of the flame indicates the presence of soda.

(*e.*) The remainder of the saline mass may be dissolved in a few drops of water, and bichloride of platinum added; if a yellow crystalline precipitate is formed, potash is present.

8. The residue which did not pass through the filter in 7 is warmed in water containing hydrochloric acid, and filtered, and we test the filtrate as follows:

(*a.*) A portion of the solution is boiled with a drop of nitric acid, and sulphocyanide of potassium is added: the development of a red colour indicates the presence of iron.

(*b.*) We treat the remainder with an excess of acetate of soda, and test with oxalate of ammonia for lime.

(*c.*) The lime being precipitated by the last operation, we filter and add ammonia to the filtrate: a white crystalline precipitate indicates the presence of magnesia in the form of phosphate of magnesia and ammonia.

* If we add perchloride of iron to a solution of phosphates, acidified with free acetic acid, we obtain a yellowish-white gelatinous precipitate of phosphate of peroxide of iron. As this compound is soluble in all acids except acetic acid, we must be careful that no other free acid is present in a solution from which we wish to precipitate the phosphoric acid by perchloride of iron. If any other free acid should be present, we treat the fluid with acetate of soda and pure acetic acid before applying the test, so as to guard against the possible solution of the precipitate.

Most of the reactions in 7 and 8 may be exhibited, although with less distinctness, in the original urine.

Tabular view of the daily urine.

(292.) We have endeavoured in the following table to bring clearly into view at a single glance the average daily excretion of the urinary constituents in an adult man of ordinary weight, viz. about eleven stone. In the case of the more important constituents, the normal maxima and minima have also been given.

| | Min. | Mean. | Max. | |
|---|---|---|---|---|
| Quantity in 24 hours | 40 | 52 | 70 | fluid oz. |
| Specific gravity | 1·005 | 1·020 | 1·030 | |
| Solid constituents | 850 | 935 | 1020 | grains. |
| Urea | 450 | 520 | 620 | „ |
| Uric acid | 4 (or less) | 8 | 15 | „ |
| Hippuric acid | | 33 * | | „ |
| Xanthine | | traces. | | |
| Hypoxanthine | | „ | | |
| Creatinine | | 7·0 | | „ |
| Creatine | | 4·5 | | „ |
| Extractive matters † | very variable, according to diet, &c. | | | |
| Chlorine | | 160 | | „ |
| (or Chloride of sodium | | 266) | | „ |
| Sulphuric acid | 23 | 32 | 38 | „ |
| Phosphoric acid | 37 | 54 | 100 | „ |
| Earthy phosphates | | 15 | | „ |
| Ammonia (?) | 4·6 | 11 | 18·6 | „ |
| Iron | | traces. | | |
| Silica | | „ | | |
| Fluorine | | „ | | |
| Gases | | undetermined. | | |

* This is Weissmann's determination for a mixed diet (see p. 305). I suspect it is far above the ordinary quantity.

† Including Scharling's oxide of omichmyle, Städeler's four acids, (viz. phenylic or carbolic acid, taurylic acid, damaluric acid, and damolic acid,) formic acid (?), butyric acid (?), urine-pigments, trimethylamine, aldehyde, &c.

(293.) Under the term *urinary sediments* we include all those substances which occur in a non-dissolved state in the urine. These substances are at first usually suspended in the fluid, but after a longer or shorter time they gradually become deposited and form a precipitate. The rapidity and completeness of the precipitate vary with the size and density of the suspended particles. To very slight sediments, consisting of extremely minute molecules, and almost disappearing on shaking the urine without rendering the fluid turbid, we often apply the term *cloud* or *cloudiness;* while, on the other hand, if the individual particles are sufficiently large to be distinguished with the naked eye, we apply the term *sand* or *gravel* to the sediment. Urinary sediments.

Urinary sediments are of such extreme importance in relation to practical medicine, that we shall notice them at considerably greater length than their mere physiological value would warrant. They frequently enable the physician to recognise at a glance important changes in the urine, which would (without their aid) require for their detection elaborate chemical processes.

The study of the urinary sediments has (as Vogel* has clearly pointed out) a double application in semecology.

(1.) From the investigation of these sediments we can draw sure conclusions regarding special changes that are going on in the general metamorphosis of the tissues of our patients. They show us that an excessive quantity of certain substances (as, for instance, uric, hippuric, or oxalic acid) is being discharged by the urine, and is consequently being produced in the organism; and they show us this by a process which involves no loss of time, and which is almost always one of absolute certainty. Importance of their study.

(2.) We recognise from their investigation certain local morbid processes going on in the uropoietic viscera. Thus, for instance, from a purulent sediment we infer that suppura-

* Anleitung z. Analyse des Harns. 3d. Ed. 1858, p. 264.

tion is occurring in some portion of the urinary organs; a sediment, consisting of cylindrical casts or tubes, informs us of certain morbid changes in the structure of the kidneys; and if the ordinary symptoms reveal the presence of stone in the bladder, we can often ascertain its nature from an examination of the gravel that is passed.

Most urinary sediments are not formed until after the urine has been discharged and has cooled; some, however, are formed in the urinary organs, and under favouring circumstances may give rise to urinary concretions. Hence it is often a point of great consequence to ascertain whether a sediment, occurring in a specimen of fresh urine, has been formed before or after its discharge from the body.

We briefly noticed in p. 296 the changes which the urine, when allowed to stand for some time, spontaneously undergoes, in consequence of the establishment in it of the acid and alkaline urinary fermentations first described by Scherer*, and the connexion between these changes and the formation of urinary sediments.

Urinary fermentation; its consequences.

The most common of all the sediments is that formed by urate of soda, which is often deposited after a short time from urine which, when passed, was perfectly clear. This deposition might arise, and often does actually arise, from the presence of so large a quantity of urate of soda in the urine, that at an ordinary temperature the whole of it cannot be retained in solution, as is shown by the disappearence of the sediment on the application of a gentle heat, or on the addition of water, or of a less concentrated specimen of urine. But it frequently happens that the urine remains clear long after its temperature has fallen to that of the surrounding air, and that a sediment of urate of soda begins to be deposited after twelve, eighteen, or twenty-four hours. The cause of the deposition in this case must, therefore, be sought for elsewhere; and Lehmann thinks that it may be traced to the pigment and extractive matters, which, according to Scherer's

* Ann. d Ch. u. Pharm. vol. xlii. p. 171.

observations, likewise occasion the deposition of free uric acid. Lehmann believes that the pigment and extractive matters increase the solubility of the urate of soda, and that their decomposition exerts an influence on this salt, and renders it less soluble. There is no doubt that the urinary pigments very readily decompose in the presence of air, and that in their decomposition a little free acid is always developed. If we expose to the air a colourless sediment containing no free uric acid, we observe that when lying moist upon a filter it assumes a beautiful red colour, and if we now try to dissolve it in water we find that it contains a certain amount of uric-acid crystals. This phenomenon is readily explained by supposing that the free acid, liberated by the decomposition of the adherent pigment, extracts from the urate of soda a little of its base, leaving a solution of the neutral salt. Lehmann believes that the urate of soda, naturally existing in the urine, is a neutral salt, and that by the abstraction (in the mode that has just been described) of a portion of its base it is converted into an acid salt or super-urate of soda.

Formation of uric-acid sediments

Scherer, in the memoir to which we have referred, has unquestionably given the true explanation of the mode of formation of uric-acid sediments; showing that they are solely dependent on the decomposition of the pigment. In perfectly fresh urine we scarcely ever see a uric-acid sediment, but every urine, as it undergoes acid fermentation, sooner or later deposits crystals of free uric acid. The free acid produced (probably) by the action of the vesical mucus on the pigment, decomposes the comparatively insoluble urates (as mentioned in the last paragraph), and by combining with a portion of the base liberates uric acid, which at once crystallises. There is reason to believe that oxalate of lime is also formed, or at all events separated during this acid fermentation; for while crystals of oxalate of lime are very seldom found in a perfectly fresh specimen of urine, they can very often be detected intermingled with uric-acid crystals after the fluid has stood for some time.

The acid fermentation having at length reached its maximum (the time varying from days to even a few weeks), the free acid gradually disappears, the surface of the fluid becomes covered with thread-like fungi, confervæ, and algæ, the reaction becomes neutral, then alkaline, and the crystals of uric acid at length disappear, and are replaced by a mixed sediment of a perfectly different nature. The ammonia produced by the decomposition of the urea throws down the earthy phosphates, the phosphate of lime falling unchanged, and the phosphate of magnesia combining with ammonia to form the beautiful and well-known crystals of phosphate of ammonia and magnesia, or triple phosphate. Another portion of the ammonia at the same time combines with the uric acid (which had formed the previous sediment), and gives rise to the production of urate of ammonia. At this stage the urine effervesces on the addition of an acid, and has almost entirely lost its original yellow tint, in consequence of the decomposition of most or all of the pigment.

Formation of phosphatic sediments.

Such is the ordinary course of the alkaline fermentation; there are, however, occasional cases in which it occurs much earlier, and without a pre-existing acid fermentation; it may even occur within the urinary bladder, in which case the urine is alkaline at the moment of its emission. (We must, however, be careful not to confound these cases with those in which the urine has been made alkaline by the administration of vegetable salts of potash or soda.)

From the preceding observations we draw the following conclusions: —

(1.) The acid fermentation consists essentially in the production of free acid (lactic, or acetic, or both) from the pigment by the catalytic action of vesical mucus, and gives rise to the deposition of: —

($\alpha$.) Free uric acid.

($\beta$.) Acid urates (chiefly urate of soda).

($\gamma$.) Oxalate of lime.

(2.) The alkaline fermentation is essentially due to the formation of carbonate of ammonia in the urine, which causes the disappearance of the sediment of uric acid, and its replacement by

(*a.*) Phosphate of ammonia and magnesia (triple phosphate).
(*β.*) Phosphate of lime.
(*γ.*) Urate of ammonia.

We may divide the urinary sediments into (1.) the unorganised, and (2.) the organised deposits.

The unorganised sediments include: —

Unorganised sediments.

Uric acid,
The urates (chiefly urate of soda),
Hippuric acid,
Oxalate of lime,
Earthy phosphates (phosphate of lime, phosphate of ammonia and magnesia),
Cystine,
Xanthine,
Hypoxanthine (formerly known as guanine),
Tyrosine.

The organised sediments include: —

Organised sediments.

Mucus and epithelial scales,
Blood-corpuscles,
Pus-corpuscles,
Cancerous and tubercular matter,
Fibrinous casts of the tubes of the kidney,
Spermatozoa,
Fungi, infusoria, &c.

We shall consider these substances in the order in which we have placed them in the preceding list.

Uric acid never occurs as a sediment except in strongly acid urine. (We are now speaking of its occurrence as an Uric acid.

ordinary sediment before the establishment of acid fermentation.) It may occur, for instance, where free lactic acid is present (see p. 22), the lactic acid decomposing some of the urates, combining with soda, and liberating free uric acid. This process may even occur within the bladder and other urinary organs. The sediment is usually of a deep yellow, a reddish orange, or a brown colour, sometimes of a pale yellow tint, but never colourless. The crystals are large enough to be recognised by the naked eye, and their form, as seen through the microscope, is shown in *Plate III, fig.* 4 (see p. 63). If in any particular case the form should not be sufficiently obvious and characteristic, we must dissolve the sediment in a drop of potash-solution on a glass slide, and add a drop of hydrochloric acid, when we shall get more distinct crystals. To separate them from urates we have only to warm the fluid, and at once filter, when the urates, dissolved by the heat, will pass through the filter, and the uric-acid crystals will be retained on it. If we wish to strengthen our microscopical proof by a chemical one, we can apply the test for the production of murexide (see p. 65).

It is very important to ascertain whether the sediment (and this remark applies equally to all the sediments whose constituents enter into the composition of urinary concretions) is formed before or after the urine has been discharged: as in the former case such urine would, unless modified by remedial agents, &c., almost certainly lead to the formation of renal or vesical calculi.

The urates.

Sediments consisting of urates are of more common occurrence than all other sediments collectively. Excepting urate of ammonia, they occur solely in acid urine. Their colour may vary from a greyish-white to a brownish-red or purple, and is considerably affected by exposure to the atmosphere. These might sometimes be mistaken at first sight for deposits of blood or pus, but the application of the murexide test, or of the microscope, or even of a gentle heat (which dissolves them,

but exerts no material change on the corpuscles of blood or pus), will remove any doubt as to their true nature.

The chemical and microscopic characters of the urates of soda, ammonia, and lime, are sufficiently given in p. 65.

The urate of soda is by far the most common of the urates; it occurs in most febrile affections, and in all conditions of the system in which the due oxidation of the blood is not effected; the urate of ammonia is of much less frequent occurrence, and is usually found in alkaline urine mixed with earthy phosphates; while urate of lime occurs very seldom, and only in small quantity.

There are two perfectly distinct conditions of the urine, in which we may have sediments of urates.

1. The daily or hourly amount of excreted uric acid may exceed the normal quantity, in which case the presence of the sediment must be referred to an increased formation of uric acid in the organism, or, at all events, to an increased separation of it by the kidneys.

2. Or if the urine be very scanty, and does not contain enough water for the purpose of solution, we may have a sediment without any augmentation of the daily or hourly amount of uric acid.

Hence we must not conclude from the presence of a sediment of urates that there is of necessity an absolute augmentation of uric acid.

We shall now endeavour to explain the causes which usually occasion the formation of a sediment of urates.

The urates being much more soluble in hot than in cold water, a urine nearly saturated with these salts will deposit them as it gradually cools; hence the reason why urine which at the moment of its discharge is perfectly clear becomes turbid on cooling. This, however, cannot explain the occasional separation of the urates within the body; and Vogel suggests that such a separation may occasionally arise from urine saturated at the moment of its secretion with urates,

becoming further concentrated in the bladder by a process of endosmosis, and thus throwing down a portion of these salts in an undissolved state.

Again, the neutral urates are more soluble than the acid urates, and these again than free uric acid. Hence any condition which converts the neutral into acid urates will occasion a deposit, provided the urine be tolerably rich in uric acid. We have already seen (see p. 355) how such an effect as this may be produced externally to the body in the acid fermentation, and the same may take place also within the body, either by the establishment of acid fermentation within the bladder (a circumstance probably of rare occurrence), or by the addition of a strongly acid urine to a faintly acid or alkaline urine, rich in neutral urates, pre-occupying the bladder.

"Sediments of the urates," says Vogel, "are of most common occurrence in acute febrile diseases or in febrile exacerbations of chronic diseases. Several predisposing causes are almost always simultaneously present in these cases: a diminution of the quantity of the urine, an absolute augmentation of the uric acid, a strongly acid reaction, and an abundance of pigment. The sediment in these cases usually appears some time after the discharge of the urine, and its deposition is occasioned partly by the cooling of the urine, and partly by the incipient urinary fermentation and the decomposition of the pigment.

"These sediments are important as indicating certain deviations from the ordinary metamorphosis of tissue, which are peculiar to most febrile diseases, namely, an increased formation of uric acid and pigment, and a diminished secretion of water by the kidneys. They are frequently regarded as critical, and as their retention in the blood gives rise to various evils, their free discharge from the circulating fluid may sometimes be deserving of the now nearly exploded epithet; too often, however, the unchecked progress of the disease shows that they have no critical significance.

"These sediments sometimes occur in perfectly healthy persons, if the above-mentioned conditions are present, as, for instance, after prolonged bodily exertion, too abundant and too frequent meals, and copious perspiration, so as to diminish the amount of urine."

Hippuric acid occasionally, although only rarely, occurs as a urinary sediment. Its crystals usually appear in the form of rhombic prisms with pointed ends (see *Plate III. fig.* 1), but sometimes are acicular. They may possibly be confounded at first sight with crystals of uric acid, or of phosphate of ammonia and magnesia, but they are readily distinguished from the latter by their insolubility in hydrochloric acid, and from the former by their not yielding the characteristic murexide reaction. Sediments containing a mixture of crystals of uric and hippuric acid sometimes occur, and Vogel states that he has occasionally seen acicular crystals of hippuric acid projecting like spikelets from larger crystals of uric acid. The two acids may be separated by boiling the mixed sediment in alcohol, which takes up the hippuric acid (which again separates on cooling), and leaves the uric acid undissolved. The necessary tests for this acid have been already given in p. 57. Hippuric acid.

The causes giving rise to the separation of hippuric acid as a sediment, are precisely the same as those which occasion the deposition of the uric acid.

Sediments of hippuric acid may occur in healthy persons after the free use of fruit containing benzoic acid or other benzoyle compounds (as for instance greengages), or after the ingestion (in any form) of benzoic or cinnamic acids.* In

* I may again direct attention to the remarkable fact already noticed in p. 305, regarding the origin of hippuric acid. Kühne discovered that during icterus no hippuric acid appeared in the urine after the administration of benzoic acid or its alkaline salts, but merely unchanged benzoic acid. This is probably due to no glycocholic acid (but merely taurocholic, or perhaps cholalic acid) being then formed in the liver; and glycine, as we have seen (page 59), appears necessary for the conversion of benzoic into hippuric acid. See a translation of Kühne's Memoir on Icterus in Beale's Archives of Medicine, vol. i. p. 342.

disease they are sometimes undoubtedly due to morbid metamorphic action: they may occur whenever there is an excess of this acid, as in the acid urine common in fever, in diabetes, in chorea, &c. Thudichum noticed a sediment of this kind in the case of a young lady suffering from colic. In the present imperfect state of our knowledge we can draw no diagnostic inference from the occurrence of a sediment of hippuric acid.

Oxalate of lime.

We have already (see pp. 7—9) noticed the chemical and microscopical characters of oxalate of lime (see *Plate I. figs.* 1 and 2). We may add that the crystals are often so small as not only to be usually invisible to the naked eye, but to require a somewhat high magnifying power to elicit their actual shape. Lehmann's statement (see p. 8) that it is often found in urine that has stood for some time, when it was not present in the perfectly fresh urine, is supported by the fact that this salt is soluble to a considerable extent in acid phosphate of soda, and we may occasionally employ the knowledge of this fact serviceably, in searching for oxalate of lime crystals; for if we are examining a very acid urine, the separation of the crystals is much facilitated by nearly saturating the free acid. It is a good plan to allow the urine to stand for some hours in a cylindrical glass, pointed or much contracted at the bottom. On carefully decanting the supernatant fluid the crystals (if there are any) will be found in the last remaining drops.

If we wish to ascertain whether urine immediately on its emission contains crystals of oxalate of lime, our only course is to filter it; and then carefully to examine with the microscope the washings of the moist filter, when if crystals of oxalate of lime be present they may be detected among an intermixture of epithelium, fibres of the filter, &c.

We have already (see p. 8) referred to the probable sources of oxalic acid in the system. It may either be introduced into the organism in the food, or as a medicine (although it

is very rarely used as a therapeutic agent), or it may be formed within either the animal or the vegetable organism, as a product of decomposition. The mode in which we can obtain oxalic acid in the laboratory by the oxidation of uric acid, and by the imperfect oxidation of sugar, starch, and compounds of vegetable acids with alkalies (tartrate, acetate of potash and soda), elucidate to a certain degree the changes which probably accompany the formation of oxalic acid in the system.

There is some difficulty in understanding how a salt so thoroughly insoluble in water as oxalate of lime, can make its way through the walls of the renal capillaries and pass into the urine. Various explanations have been attempted. C. Schmidt assumes that oxalate of lime forms a soluble compound with albumen; that in this form it exists in the blood and passes into the urine; and, finally, that in the urinary passages this compound is decomposed, and that the liberated oxalate of lime then separates as a sediment. Another explanation assumes that the oxalic acid, formed by the decomposition of the tissues, does not combine with lime till it has entered the urinary organs. A third (and perhaps the best) explanation is afforded by the observations and experiments of Kletzinsky, who remarked that oxalic acid and lime when brought together in a state of extreme dilution, require the lapse of a certain time before they unite to form an insoluble oxalate.*

The importance of oxalate-of-lime sediments, in reference

* The following experiments bearing on this point were made by Kletzinsky. He added oxalate of ammonia to urine which had been strongly acidulated with acetic acid. After passing this fluid through four filters, he observed after a short interval a slight crystalline turbidity arising from the oxalate of lime in the previously clear fluid. He likewise introduced some of the above-mentioned fluid into an endosmometer closed with a piece of bladder which dipped down into pure tepid water. In the course of ten hours he found crystals of oxalate of lime in the water outside the bladder. The lime-salt and the oxalate of ammonia had here obviously been diffused through the membrane in a state of indifference to each other, and had only combined to form oxalate of lime after their escape from the endosmometer.

to diagnosis and medical treatment, varies very much according to the conditions under which such sediment occurs. Vogel arranges these conditions in the two following groups: —

(1.) There are cases in which the urine continuously, for weeks or even months, contains large quantities of oxalate of lime. This is the condition to which the terms oxaluria and oxalic diathesis have been applied by some writers. There are two perfectly different dangers to be apprehended in such cases.

(*a.*) A renal or vesical concretion of oxalate of lime (the mulberry calculus) may be formed.

(*b.*) Bad consequences may result from the poisonous action of the oxalic acid on the digestive organs and the organism generally, especially on the heart and nervous system.* Beneke attempts to explain the noxious action of the oxalic acid chemically. He believes that it dissolves the phosphate of lime and removes it from the system, and that from the loss of phosphate of lime thus induced, there is a diminution in the formation of organic cells in the various organs. The ordinary causes of this excessive formation of oxalic acid in the system, seem to be disturbances of the respiratory functions, with diminished absorption of oxygen, a too abundant use of sugar, and probably many other conditions giving rise to derangements of the ordinary metamorphic action going on in the various tissues.

(2.) Again, there are cases of quite a different kind, in which we either find mere traces of oxalate of lime in the urine, or where its more abundant appearance is merely transitory, as during various acute and chronic diseases. In these cases there is comparatively little to fear.

Sediments of earthy phosphates almost always consist of

* The consequences arising from the accumulation of oxalic acid in the blood are very well described in a paper by Dr. James Begbie, "On Stomach and Nervous Disorder, as connected with the Oxalic Diathesis," in the Monthly Journal of Medical Science, August, 1849.

an admixture of phosphate of lime, and phosphate of ammonia and magnesia. In consequence of their very ready solubility even in very weak acids, they can never occur in a urine presenting an acid reaction, and we only meet with them in neutral or alkaline urine. Earthy phosphates.

Phosphate of lime occurs in sediments, as an amorphous powder insoluble in water, but soluble in acids, from which it is again precipitated by alkalies. In normal urine it is held in solution by the free acid. (In those cases in which it is precipitated by heat, it had most probably been dissolved by carbonic acid).

Phosphate of ammonia and magnesia is not a normal constituent of the urine, but always appears in singularly beautiful crystals as soon as that fluid becomes alkaline. In certain grave forms of disease of the bladder, and of the spinal cord, sediments consisting solely of these crystals are often noticed, and Lehmann once saw a similar sediment in a case of diabetes. (See *Plate IV. fig.* 5.)

These crystals of phosphate of ammonia and magnesia may generally be at once recognised by these forms. They most frequently present shapes which are modifications of rhombic vertical prisms, and somewhat resemble, and have been compared to coffins. They are insoluble even in hot water, but dissolve readily in acetic acid, by which means they may be distinguished (if necessary) from crystals of oxalate of lime. They are not affected by alkalies.

Since the phosphates of lime and magnesia occur in normal urine (see p. 321) in the ratio of two to one, we may conclude that this is nearly the ratio in which these earthy sediments are composed.

When the alkalinity of the urine is due to the administration of liquor potassæ or of carbonate of potash or soda, and not to the presence of carbonate of ammonia, the sediment consists solely of phosphate of lime and magnesia, without any crystals of triple phosphate.

If the earthy phosphates are mixed with other sedimentary matters, we may be assisted in their recognition by recollecting; (1.) that urates are readily soluble in hot water, while the phosphates are insoluble; (2.) that acetic acid will enable us to distinguish between phosphate of ammonia and magnesia, and certain somewhat similar forms of oxalate of lime; and (3.) that free uric acid cannot occur in the neutral or usually alkaline urine, which contains a sediment of earthy phosphates.

We have no right to infer from the presence of a sediment of earthy phosphates, that these substances exist in excess in the urine, for every urine, when it becomes alkaline, throws down such a sediment (see p. 356). We can only decide whether there is an actual augmentation of the earthy phosphates by a quantitative analysis of the urine with respect to them; but an easy method has been suggested by Beneke for their approximate determination, the details of which are given in the foot-note.*

Independently, however, of any quantitative analysis of

* By saturating the free acid of the urine by any alkali, we obtain the precipitation of any earthy phosphates that may be contained in it; and from the amount of turbidity that ensues, we can approximately determine the amount of the earthy phosphates. Beneke recommends that cylindrical test-tubes of the same size, and having a mark or line indicating the half-ounce fluid measure, together with a soda solution of known strength (one part of soda to twelve of water) should be employed: and he uses a numerical scale, containing seven magnitudes, to indicate seven different degrees of turbidity.

By 0 he indicates a urine which exhibits no turbidity whatever after half an ounce has been boiled in a test-tube, and five, ten, or fifteen drops of the soda-solution have been added.

By $\frac{1}{2}$, a urine which when similarly treated exhibits a slight opalescence.

By 1, a urine which exhibits a strong opalescence, but is still sufficiently transparent to allow us to see certain objects (as the bars of a window) through it.

By $1\frac{1}{2}$, a more opalescent urine, through which objects can no longer be distinguished.

By 2, a urine which is strongly turbid — more than opalescent.

By $2\frac{1}{2}$, a urine which, a few seconds after the addition of the soda, yields a considerable precipitate of earthy phosphates.

By 3, a urine which at once forms a copious precipitate.

By 3–4, a urine which throws down the largest possible quantity of earthy phosphates on the addition of the soda.

the earthy phosphates, their mere presence often serves to direct our attention to the fact that the urine is alkaline, and in that respect is of diagnostic importance. Having ascertained, either by this means or by ordinary test-paper, that the urine is alkaline, we have to investigate the cause of that abnormal reaction.

Various causes of an alkaline reaction of the urine.

(1.) The alkaline reaction may be due to carbonate of ammonia, which (unless in the comparatively rare cases in which that salt has been prescribed, and has passed directly into the urine) always depends upon the decomposition of urea, and is usually associated with blennorrhœa or pyorrhœa.

In this case red litmus-paper moistened in the urine becomes blue, but regains its red colour on drying.

(2.) Or the alkaline reaction may depend on the presence of a fixed base (potash or soda) or of an alkaline earth. The cause of the reaction in these cases may be referred

(*a.*) To the medicinal use of the caustic alkalies, of the alkaline earths, or of their carbonates, tartrates, acetates, &c.

(*b.*) Or to the use of food rich in some of these compounds (certain fruits, for instance, as strawberries, &c.)

(*c.*) Or to certain modifications in the metamorphosis of tissue.

In these cases red litmus-paper moistened in the urine becomes blue, and remains so after drying.

With regard to the practical value of the alkalinity of the urine in relation to the prognosis and treatment of a case,

Beneke has ascertained by careful experiments that one fluid ounce of urine

| of scale | | | | | | |
|---|---|---|---|---|---|---|
| 0 | contains from | 0·10 | to | 0·15 | of a gramme of earthy phosphates. | |
| ½ | „ | 0·25 | „ | 0·30 | „ | „ |
| 1 | „ | 0·40 | „ | 0·45 | „ | „ |
| 1½ | „ | 0·55 | „ | 0·60 | „ | „ |
| 2 | „ | 0·70 | „ | 0·75 | „ | „ |
| 2½ | „ | 0·85 | „ | 0·90 | „ | „ |
| 3 | „ | 1·00 | „ | 1·05 | „ | „ |
| 3–4 | „ | 1·00 | „ | 1·30 | „ | „ |

Hence we can readily approximate to the daily excretion of the earthy phosphates.

Vogel remarks, that if the disappearance of the normal acid reaction is only transitory; if it only occurs at one period of the day, as for instance some hours after the principal meal, or after certain kinds of food, or only on occasional days, the indication is rather of physiological than of practical interest. If, on the other hand, the urine is frequently or always alkaline, the indication is of great diagnostic and practical value. If the urine is ammoniacal, and contains pus or mucus and crystals of phosphate of ammonia and magnesia, we diagnose a blennorrhœa or pyorrhœa of the urinary passages. If it is alkaline without being ammoniacal, and we cannot trace this condition to the use of medicines or peculiarities of food, we must refer it to certain modifications in the metamorphosis or disintegration of the tissues, regarding which we have little definite knowledge, but which seem especially to occur when there is imperfect metamorphosis of the muscular tissue, want of tone in the nervous system, anæmia, chlorosis, and imperfect nutrition, and under a depressed condition generally.*

It would be altogether out of place here to enter into details regarding the treatment in cases of alkaline urine; but it may be well to observe that the common practice of (on false chemical grounds) prescribing acids often leads to very bad results, as might, indeed, be foretold if we recollected that the alkalinity of the urine is often primarily dependent upon the irritation established by too acid an urine on the delicate mucous structures with which it comes in contact.

When the urine on its emission contains a sediment of earthy phosphates, these salts must obviously have been separated within the urinary cavities, and if this phenomenon

* Rademacher, the author of an ingenious but vague system of medicine, remarked that ferruginous preparations were the proper remedies for cases of constantly alkaline urine. Vogel remarks, that this statement requires some limitation. Pale urine is a much more certain indication that iron is required, and, as has been already mentioned, urine with little pigment has a great tendency to become alkaline.

should continue for any length of time, the formation of a concretion in the kidney or bladder would probably result.

Cystine occasionally, but very rarely, forms a urinary sediment. It may be readily separated from an admixture of urates and of the earthy phosphates by boiling, and by the addition of acetic acid, which dissolve everything but the cystine. Its microscopical and chemical tests are sufficiently given in page 51. Cystine.

An interesting notice of cystine-formation has recently been recorded by Toel.* Two otherwise healthy sisters (except that they had occasional pain in the region of the kidneys, due, probably, to a renal calculus of cystine) passed urine containing a sediment of cystine. This sediment was most abundant in the morning urine †, and the total excretion averaged more than a scruple daily. There is reason to believe that the formation of cystine is occasionally an hereditary peculiarity.

The probable origin of cystine is sufficiently noticed in page 52. In the present imperfect state of our knowledge we can draw no diagnostic inferences from its presence, except that there is possibly a cystine-concretion in the kidney or bladder.

Xanthine and guanine may possibly occasionally be constituents of urinary sediments. As far as I know there are, however, no recorded cases of their thus occurring.

We now come to the consideration of the organised sediments.

Every urine contains more or less mucus, which is derived from the mucous membrane of the uropoietic viscera, and which, when the urine is allowed to stand, soon falls down in the form of a cloudy sediment.‡ On examining such a Mucus and Epithelium.

* Ann. d. Ch. u. Pharm. vol. xlvi. p. 247.

† The same was observed in a specimen of urine containing cystine analysed by Dr. Beale. See Archives of Medicine, vol. i. p. 136.

‡ I have previously alluded to the part which mucus plays in causing the

sediment under the microscope we usually find distinct nucleated epithelial cells, derived from the walls of the bladder, and round, more or less granular, mucus-corpuscles (cytoid corpuscles).

It must be recollected that pus-corpuscles may be converted in ammoniacal urine into a gelatinous magma, which very closely resembles a mucous sediment.

The diagnostic indications of an excess of mucus are too obvious to require notice.

Pus.

Pus can only be recognised with certainty by the microscope, under which (with a sufficient magnifying power, of about 250 diameters) its corpuscles are seen as round, pale, faintly granular bodies of varying sizes, which become transparent on the addition of dilute acetic acid, and then distinctly reveal a very characteristic nucleus, which was previously much less apparent. (See p. 390.) Their distinctly granular appearance, and their behaviour with acetic acid, serve to distinguish them from blood-corpuscles.

Any considerable quantity of pus in urine always forms a sediment. When it is only sparingly present, the urine must be allowed to stand for some hours in a tolerably long test-tube, and the last drops, after careful decanting, must be placed under the microscope. The effect of ammoniacal urine, to which we have previously alluded, must not be forgotten in the search for pus; for in the gelatinous magma, to which we have there referred, the shape and outlines of the pus-corpuscles entirely disappear. Every purulent urine is of course more or less albuminous, from the occurrence of the serum of the pus.

The presence of pus in the urine is always an indication of suppuration of some part of the uropoietic viscera, or of an

decomposition of the urea: Scherer has demonstrated the correctness of this view by removing the mucus from fresh urine, either by filtration or by the addition of alcohol; the urine then retains its acidity for a very much longer time than ordinary.

abscess communicating with them, except when (in women) it sometimes makes its way into the urine from the vagina or uterus.

It is often by no means easy to determine the seat of suppuration. Vogel remarks that when the pus arises from the urethra, pus is usually discharged at other times than those of micturition; if it arises from the bladder there are usually certain symptoms (local pain, &c.) indicative of disease of that viscus; if it arises from one or both ureters, colic-like pains are felt in the region of those ducts, while suppuration of the parenchymatous structure of the kidney is often accompanied with little or no local disturbance. We are further assisted in deciding whether pus arises from a mere superficial inflammation of the mucous membrane or from deeper seated disease, by recollecting that if the appearance of pus in the urine is transitory—lasting only for a few days—the pus is probably only the result of a superficial inflammation, while, if it is persistent, it probably originates in a deeper source; and by the appearance, under the microscope, of the corpuscles: for pus, from a superficial source, presents the corpuscles in their normal (perfectly spherical) form, and with clearly defined characteristic nuclei (as shown by the addition of acetic acid) while in deeper seated suppuration there are often various deviations from the normal type, both the corpuscles and their nuclei presenting more or less want of definite character.

Cancerous and tubercular matters.

Cancerous and tubercular matters sometimes occur in the urine, and their detection is obviously of great diagnostic importance to the physician, as indicating that a cancerous or tuberculous deposit, in some portion of the uropoietic viscera is in the stage of softening and disintegration.

When cancer-cells occur in the urine they much more commonly arise from cancer of the bladder than from cancer of the kidneys. The cancer is usually the soft or medullary kind, and the cells found in the urine generally occur aggregated in small masses, presenting the various modifications

of form and shape which are found in cancerous formations.*

Tubercular matter, when it occurs in the urine, closely resembles pus, from which it cannot be distinguished without the aid of the microscope. It consists of irregular and imperfectly developed pus-corpuscles, fragments of cells, detached nuclei, and an indistinct finely granular matter, in which broken crystals of cholesterin may sometimes be detected. In these cases the tubercular matter is deposited in the mucous or submucous tissue of some portion of the urinary tract.

Tubular casts.

In certain forms of disease affecting the parenchyma of the kidneys, peculiar, elongated, tubular, or cylindrical bodies are observed on instituting a microscopic examination of the sediment. They mainly occur in the three following forms: —

(1.) Epithelial tubes. These are tubular aggregations of epithelial cells, precisely like those which we obtain from the medullary portion of a fresh kidney, and consist of the epithelium of the uriniferous tubes (the tubes of Bellini), which is detached in patches by a morbid process, and is thus discharged with the urine. Together with these larger tubes, we often find cylindrical epithelium from the calyces, or the pelvis of the kidney, and occasionally pus-corpuscles.

(2.) Granular cylinders. These are solid, granular, cylindrical masses, similar in form and size to the first variety. We can sometimes see detached epithelial cells, blood-globules, pus-corpuscles, or oxalate-of-lime crystals in their interior.

(3.) Hyaline cylinders. These, like the preceding, are solid cylinders, but so pale and transparent that it requires considerable tact to distinguish them, under the microscope, from the surrounding fluid. They may be rendered more distinct by adding to the urine a few drops of a solution of iodine in iodide of potassium, which gives them a brownish tint.

* See Vogel's Pathological Anatomy (translated by the author of this work) for the best account of the Histology of Cancerous Formations.

Since these tubes and cylinders often occur only in small number, we must, if we wish to determine whether any are present, adopt one of the two following courses: — we must either allow the urine to stand for a considerable time, and then examine the sediment, or else we must filter it, and examine the contents of the filter. In doubtful cases the iodine solution should be added so as just to colour the urine. Structures are occasionally found in urinary sediments, which may easily be mistaken for granular cylinders, but which seem to be aggregations of molecular particles in a cylindrical form: they occur, for the most part, in albuminous urine, or in urine which has stood till decomposition had commenced, and are apparently composed of albumen, and possibly mucus, precipitated in a finely granular state. They have a less regular form than the true granular cylinders.

The detection of these tubes and cylinders is of great diagnostic importance, since they always originate from the tubular structure of the medullary portion of the kidney (the tubes of Bellini), and indicate that certain morbid processes are going on there. They are sometimes regarded by inexpert pathologists as a certain sign of Bright's disease, but Bright's disease is no longer associated with a single morbid condition of the kidney; and farther, the epithelial tubes and the granular and hyaline cylinders indicate the presence of very different processes in that organ.

The presence of epithelial tubes in the urine shows that the epithelium is peeling away from the tubes of Bellini—in short, that there is desquamative nephritis, a process which may disappear in a few days, without leaving any bad consequences. When, however, pus-corpuscles are intermingled with the epithelial tubes, we may infer that there is more or less intense inflammation of the renal structures. These tubes are most commonly observed in the beginning of granular degeneration of the kidney, and in the desquamative stage of erysipelas and scarlatina.

The granular and hyaline cylinders are indications of a more serious, and a chronic affection of the parenchymatous structure of the kidney. The hyaline cylinders are probably formed by an exudation and subsequent coagulation of a fibrinous fluid upon the inner surface of the tubes; in short, by a croupous exudation; while the granular cylinders are formed, either by a subsequent metamorphosis of the fibrinous effusion, or by the degeneration of the glandular epithelium which lines the uriniferous tubes.

The number and persistence of these structures in the urine are usually proportional to the severity of the morbid process.

When the cylinders contain much fatty matter (and both fat-globules and fatty granules are often enclosed in them), we may infer that the morbid process going on in the kidney is fatty degeneration.

If blood-globules are frequently contained in the cylinders, or if blood is mixed with them, we may infer the presence of fatty or lardaceous degeneration of the minute vessels forming the Malpighian bodies.

If the cylinders present either a very small or a very large diameter, we infer in the former case a contraction, and in the latter a dilatation of the uriniferous tubes; while if the cylinders deviate from their normal form, and present constrictions and dilatations, we may infer that the tubes in which they were formed are in a varicose state.

Fungi.

Fungi, not unlike the *Mykoderma cerevisiæ* in shape, but considerably smaller ($\frac{1}{280}$th to $\frac{1}{330}$th of a line), commonly occur in stale urine; and sometimes, viz., when in cases of vesical catarrh, the urine has undergone incipient decomposition before emission, they may be detected in the freshly discharged fluid. Their presence is of no special diagnostic importance if we except the yeast-plant (*Myk. cerev.*), which in a tolerably warm atmosphere is always developed spontaneously in diabetic urine. (See *Plate V. fig.* 1.)

I am not aware of any cases in which Infusoria have been detected in perfectly fresh urine, although monads and vibriones are sometimes developed in an extremely short time, indicating a great depression of the vital powers, and a septic condition of the organism. Dr. Hassall has recently described the occurrence of an infusorium of the genus Bodo, in the urine; and Goodsir's Sarcina ventriculi * has been observed in a few cases. Infusoria.

Spermatozoa sometimes occur in the urine from obvious and natural causes. They are stated to have been detected in the urine in cases of typhus, and Lambl has suggested that the presence of a catheter as it passes the prostate, especially if a digital examination *per anum* is being simultaneously made, may cause their appearance in the urine. Spermatozoa.

(294.) The following general *resumé* of the preceding remarks on the urinary sediments may serve to facilitate the microscopic recognition of the individual varieties. Tabular resumé.

A. The urine *acid.*

(1.) The sediment entirely *amorphous.* We warm a drop or two on an object-glass.

(*a.*) If, as is probable, there is perfect solution, the sediment consists of urates (almost certainly acid urate of soda.) If we add a drop of acetic or hydrochloric acid, rhombic tablets of uric acid soon appear. (See *Plate III. fig.* 4.)

(*b.*) If glistening, strongly refracting globules are intermingled with the sediment, and they are found to be soluble in ether, they consist of fat.

(2.) The sediment partly or entirely *crystalline.*

(*a.*) Minute glistening perfectly transparent octohedral crystals, presenting much the appearance of the front of a letter envelope, and insoluble in acetic acid, are oxalate of lime. (They sometimes require a magnifying power of 300 or 400 diameters.) (See *Plate I. fig.* 1.)

* Welcker suggests that the sarcina found in the urine is a distinct species from that found in the stomach.

(*b.*) Four-sided tablets, which by the rounding off of their oblique angles sometimes present fusiform or barrel-like shapes, and which are always more or less coloured, are uric acid. If there is any doubt, we dissolve the crystals in a little potash or soda solution, and add a drop of hydrochloric acid, when we are sure to get sufficiently characteristic forms. (See *Plate III. fig.* 4.)

(*c.*) Regular hexagonal plates, which are soluble in hydrochloric acid (from which they are again precipitated by carbonate of ammonia), and soluble in ammonia (from which they are again precipitated by acetic acid), are cystine. (See *Plate II. fig.* 7.)

(3.) The sediment containing *organised bodies.*

(*a.*) Twisted bands consisting of series of rows of the most minute granules are coagula of mucus, often accompanied with urate of soda. They must not be confounded with the cylinders described in pp. 372–4.

(*b.*) Small granular corpuscles, which are generally grouped together into shield-like masses, are mucus-corpuscles.

(*c.*) Circular, slightly biconcave discs, usually of a faintly yellow colour, which at once swell and after a short time dissolve in acetic acid, leaving no nucleus, are blood-corpuscles. If they have been for any length of time exposed to the action of the surrounding fluid, they are often angular, jagged, and irregular.

(*d.*) Pale, granular, spherical globules of various sizes, which swell and become transparent in acetic acid, and then reveal distinct and characteristic nuclei, are pus-corpuscles.

(*e.*) Tubular cylinders can only be the casts described in pp. 372–4.

(*f.*) Epithelial cells, varying according to their origin. (*aa*). If they are roundish, elongated, or polygonal cells, with tolerably distinct nuclei, they come from the bladder. (*bb.*) If they are club-shaped and fusiform caudate cells, they come from the ureters or the kidney.

(*g.*) Minute fungi generally occur in urine in which acid

fermentation is commencing. They commonly appear as minute nucleated cells, which increase by gemmation, and thus form single or branching rows. Other forms are sometimes seen.

(*h.*) Short thin rods wriggling through the fluid are vibriones. (They are far less common in acid than in alkaline urine.)

(*i.*) The Sarcina ventriculi (of very rare occurrence in the urine) cannot be mistaken for anything else.

(*k.*) Spermatozoa are recognised by their tadpole-like shape. For their detection we require a somewhat high power.

(*l.*) Cancerous and tubercular matters (see p. 371).

B. The urine *alkaline.*

The sediment containing *crystals.*

(*a.*) If there are various combinations of rhombic vertical prisms, which are soluble in acetic acid, and which, on being warmed with a solution of soda, develope ammonia, they are phosphate of ammonia and magnesia. Their peculiar microscopic form is generally quite sufficient for their recognition, without even the addition of acetic acid. — See *Plate IV. fig.* 5.

If oxalate of lime is simultaneously present, it is brought clearly into view by the addition of a drop of acetic acid.

(*b*). Small dark spherical masses studded with minute projecting acicular crystals, are urate of ammonia. (See *Plate III. fig.* 6.)

The sediment containing *amorphous* matter.

In an alkaline or a neutral urine this is almost certainly phosphate of lime, in which case a drop of hydrochloric acid will dissolve it.

The sediment containing *organised* bodies.

The same bodies occur here as in acid urine, but this is the more natural *habitat* for fungi and infusoria.

Urinary concretions.

(295.) Urinary concretions may be formed either in the kidney or in the bladder, and are almost always the result of the deposition and retention of a urinary sediment in some portion of the uropoietic tract. Around the nucleus thus

formed additional matter is gradually deposited, till at length the concretion may attain an enormous size.

In consequence of the serious and often perilous disturbance established in the system by the presence of a urinary calculus, it is of great importance that we should not only be able to detect, at a very early stage, the existence of such a concretion, but also that we should be able to ascertain its chemical composition; for with a knowledge of the latter point, we can at all events usually prevent its further enlargement, although we have hitherto been seldom successful in effecting the solution of an existing calculus within the bladder.

Their constituents.

The chemical constituents of urinary calculi are essentially the same as those of the urinary sediments which have been already described, namely:—

Uric acid and urates,
Xanthine,
Cystine,
Oxalate of lime,
Carbonate of lime,
Phosphate of lime,
Phosphate of magnesia and ammonia,
Protein-compounds (fibrin, mucus),
Urostealith,

with occasional traces of silica, alumina, &c.

Many concretions consist solely of one of the above constituents (especially of uric acid and of oxalate of lime) whilst several constituents enter into the composition of others; in the latter case the different constituents usually occur in strata or layers.

To ascertain the true nature of a calculus we must saw it through the centre; the section at once shows us whether the external parts are identical with, or differ from the central portion or nucleus. If the calculus is built up of various

strata, a portion of the powder of each stratum must be analysed.

(1.) If the portion of the concretion which we examine is entirely combustible, when exposed in a platinum spoon, or on a piece of platinum foil, to the heat of a spirit-lamp, or if it merely leaves a very slight residue, it must consist of one or more of the following substances: — Combustible calculi.

Uric acid or urate of ammonia,
Xanthine,
Cystine,
A protein-substance, or
Urostealith.

In order to determine of which of the above substances the pulverised concretion consists, we proceed as follows: —

We first test for uric acid. If with nitric acid and ammonia we obtain a distinct murexide-reaction (see p. 65), the concretion consists either of uric acid or urate of ammonia. The latter may be distinguished from the former by its much greater solubility in boiling water, from which it again precipitates on cooling, and by its developing ammonia on the addition of a solution of potash or soda. Of the two, uric acid calculi are by far the more common. Indeed, they are the most common variety of calculi. They frequently attain a considerable size; are generally of a yellow, reddish, or reddish-brown colour (seldom white), usually present a smooth surface, and are tolerably hard in their consistence. Calculi formed of urate of ammonia, are rare and generally only small; they are also of a lighter colour and a more earthy consistence than uric acid calculi. Uric acid.

If the concretion is combustible and does not yield the murexide-reaction, it must consist of xanthine, cystine, a protein-substance, or urostealith.

Xanthine (or xanthic oxide) dissolves in nitric acid without any evolution of gas, and, after evaporation, leaves a bright Xanthine.

lemon-coloured residue, which is not reddened by ammonia, but dissolves with a deep reddish-yellow colour in potash-solution.

Calculi of xanthine are extremely rare, only three authenticated cases having been placed on record as occurring in man. They are of a light brown cinnamon colour, tolerably hard, assume a waxy appearance when rubbed, and usually consist of concentric, easily detachable layers.

Cystine. Cystine calculi are by no means common, although not nearly so rare as the preceding variety. They are of a dull yellow colour, have a smooth surface, and when broken present a glistening conchoidal fracture. They are soft enough to admit of being readily scraped, and their powder communicates a soapy feeling to the fingers.

In addition to the chemico-microscopical tests for cystine, mentioned in p. 51, we may notice the following test proposed by Liebig, which is based on its large percentage of sulphur.

If a calculus, containing cystine, be dissolved in potash-solution, and if a little solution of acetate of lead be added, and the mixture boiled, a black precipitate of sulphide of lead is formed, which gives to the fluid the appearance of ink.

Fibrinous calculi. Calculi, consisting of protein-substances (fibrin or coagulated blood), are very rare. They present no signs of crystallisation, evolve on combustion an odour of burned horn, are insoluble in water, ether, and alcohol, but dissolve in potash-solution from which they are precipitable by acids; they are also soluble in boiling nitric acid.

Urostealith. Calculi of urostealith * have only been observed in three

* For further particulars regarding this very rare form of urinary concretion I may refer to my translation of Simon's Animal Chemistry, vol. ii. pp. 326 and 452, in which I have given a full abstract of the views of Heller, its discoverer. Dr. W. Moore has subsequently published a notice of two cases in the Dublin Quarterly Journal of Medical Science, for March 1854, vol. xvii. p. 473; and another seems recently to have occurred in the practice of Pro-

or four cases. In their fresh state they are soft and elastic, and feel to the hand like india-rubber. When dried they contract, become darker in colour, and hard, but again soften on warming. On heating a fragment on platinum foil, it fuses and swells up, and gives off a pungent odour, resembling that of shellac and benzoine; it then takes fire, and burns with a clear yellow flame, leaving a voluminous carbonaceous residue. It dissolves with difficulty in hot alcohol, but readily in ether. Its elementary composition is entirely unknown; but it is apparently a resin or a fat.

Incombustible calculi.

(2.) If the concretion is incombustible or leaves a considerable residue after exposure to a strong heat, it may consist of —

Urates with a fixed base (soda, magnesia, lime).
Oxalate of lime.
Carbonate of lime.
Phosphate of lime, or
Phosphate of magnesia and ammonia.

The urates.

The urates of soda, magnesia, and lime never, either alone or in association with one another, are the sole or even principal constituents of a urinary calculus, but they sometimes occur in various quantities in calculi consisting mainly of uric acid or urate of ammonia.

To ascertain whether these bases are present in combina-

fessor Santesson of Stockholm, whose "Cases in Surgical Practice," have lately (August 24th, 1859) been translated by Dr. Moore for "The Dublin Medical Press." Neither Professor Santesson nor the chemist who examines the calculi in question seems to have heard of urostealith. They describe the nucleus as consisting of "a fat which was its chief constituent, in combination with some lime," and believe that it has arisen from the metamorphosis of coagulated blood. I agree with Dr. Moore in thinking that the nucleus was Heller's urostealith, and it is not improbable that their suggestion regarding its origin is correct. Many years ago my friend, Dr. Henry Bennet, brought me a small oval mass of a yellow colour and tolerably soft consistence, which was passed from the bladder of a female patient of his; and which I strongly suspect was the substance in question.

tion with uric acid, we boil a portion of the powdered calculus and filter while hot; on evaporation we obtain these urates if they are present, and by incinerating the residue thus left, we obtain the fixed bases. If they render moistened turmeric paper brown, potash or soda must be present, and the latter may be identified by the yellow tinge which it gives to the flame of the blow-pipe. Unless the heating has been much prolonged, the magnesia and lime will occur in the ash as carbonates, which are insoluble in water, but dissolve freely in dilute acids, from which they may be precipitated as phosphate of magnesia and ammonia, and as phosphate of lime, by an addition of phosphate of soda, and of ammonia.

Oxalate of lime.

Oxalate of lime blackens on exposure to a strong heat, in consequence of the charring of its organic matter (mucus), but by prolonged exposure to heat it becomes white, without fusing. By strong and prolonged heat it is reduced to caustic lime, which communicates a brown tint to moistened turmeric paper; when exposed to a less amount of heat it is only reduced to carbonate of lime, which dissolves with effervescence in dilute hydrochloric acid. On neutralising this solution with ammonia we obtain no precipitate, but by the farther addition of oxalic acid, or by at once adding oxalate of ammonia, oxalate of lime is again precipitated, which, if we wish to carry our tests farther, is found to be insoluble in boiling water, in acetic acid, and in potash solution, but to dissolve in hydrochloric or nitric acid without effervescence.

Calculi of oxalate of lime are not uncommon, especially in children. They are sometimes small, of a pale colour, and smooth, when they are known as hemp-seed concretions; while more commonly they are larger, of a darker colour, rough, and even nodular, when they are known as mulberry calculi.

Carbonate of lime.

Calculi composed solely or mainly of carbonate of lime are rare in the human subject, but common in herbivorous

animals. In the few cases in which they occur they have been generally found to be small and numerous, and to present a whitish chalk-like character. Carbonate of lime is often found in comparatively small quantity in calculi consisting chiefly of oxalate of lime or earthy phosphates.

Concretions of carbonate of lime blacken upon exposure to a strong heat, in consequence of the mucus, &c., which is usually contained in them, but subsequently become white. The remarks made on the chemistry of oxalate of lime afford the necessary information for the recognition of carbonate of lime.

Fusible calculi.

Phosphate of magnesia and ammonia, and basic phosphate of lime usually occur together in urinary calculi, which have originated from the urine becoming ammoniacal within the bladder. They often attain a considerable size, usually have a whitish colour, and are soft, porous, and chalky, when the phosphate of magnesia and ammonia preponderates, and are comparatively hard and dense when the phosphate of lime is in excess.

When exposed to a strong heat they become fused into a white enamel-like mass, and from this characteristic property they have received the name of fusible calculi. Moreover, no amount of heat will render their reaction alkaline, which likewises serves to distinguish them from oxalate and carbonate of lime. They are soluble in hydrochloric acid without effervescence, both before and after exposure to heat, and, in the latter case, the solution is precipitated by ammonia.

If we wish to separate the two phosphates from one another we must dissolve the powdered fused mass in dilute hydrochloric acid and filter. We must then add ammonia to the filtrate till only a faintly acid reaction remains, or, if we add too much ammonia, so as to render the solution neutral or alkaline, and consequently turbid, we must dissolve the precipitate by the addition of a few drops of acetic acid. If we now add oxalate of ammonia, the lime (alone) is preci-

pitated as an oxalate, while the phosphate of magnesia and ammonia remains in solution. To obtain the latter salt we must remove the lime by filtration, and then supersaturate with ammonia.

The above-named ingredients of calculi often occur in various combinations; thus we sometimes find earthy phosphates associated with uric acid and urates, and sometimes with oxalate of lime; and calculi have been analysed which contain no less than six different ingredients, viz.: uric acid, urate of ammonia, oxalate of lime, phosphate of lime, carbonate of lime, and phosphate of magnesia and ammonia. The various constituents are sometimes intimately intermingled with one another, and sometimes deposited in separate and distinct strata; in the latter case having been obviously deposited at different times, in consequence of a change having occurred (often from the administration of alkalies or their carbonates) in the acidity or composition of the urine. If, for instance, in a case of the so-called uric acid diathesis, the urine is sometimes strongly acid, so as to decompose the urates, and then for a time less acid, or even neutral, so that undecomposed urates are deposited, we have the necessary conditions for a calculus with alternate layers of uric acid and urates; and the earthy phosphates, which so often form an outer coating to a mulberry calculus, owe their origin to urine having become ammoniacal from the irritation set up in the bladder by the stone.

# CHAPTER XV.

## EXUDATIONS.—PUS.

(296.) Exudations in many respects resemble the transudations described in Chap. XI. Sect. iv., and the two classes of fluids have not been sufficiently separated by some writers on Pathology. As we shall shortly see, they essentially differ from one another in their origin, in the mode in which they are separated from the blood, and in their physical and chemical properties. Characteristics of exudations

The formation of transudations is dependent on simple physiological laws (see p. 258). In transudations certain constituents of the blood-plasma permeate the walls of the capillaries, partly in consequence of increased penetrability of these walls, and partly in consequence of the plasma having an increased diffusion-power, and we have no actual stasis of the blood in the capillaries; while exudations arise as a consequence of inflammation (of a perfect stasis of the blood in the capillaries) and partial rupture of the vessels. Difference between transudations and exudations.

In exudations we always find very considerable quantities of fibrin, and far more albumen than in transudations, the phosphates and potassium-compounds are also in excess in the former, and blood-corpuscles (more or less modified in form) are also present, which is never the case in true transudations. But the principal point of difference between the two is that the former have a great capacity for undergoing further changes, and for developing cells and tissues, while the latter will remain almost entirely unchanged for a great length of time in the cavities in which they were originally effused. The substances, whose presence in exudations gives

rise to their plasticity, and whose absence from transudations seems to deprive the latter fluids of this property, probably are fibrin, phosphates, and the hæmatocrystallin which passes into the exudations with the blood-corpuscles.

Cause of their plasticity.

The commonly received view that the plasticity of the exudations is essentially dependent on their fibrin, is strongly opposed by the fact that in certain transudations (as, for instance, in acute dropsy) there is an abundance of fibrin, and yet no morphotic elements are produced; and we are hence led to suspect that this plasticity must be in some way connected with the escaped contents of the destroyed blood-corpuscles. The phosphates again probably assist in conferring this property on exudations, for we universally find (even in the lower animals, whose organisms are relatively poor in such salts) that, wherever cells and fibres are formed, phosphates are accumulated in appreciable quantity; and it has likewise been ascertained that the blood returning from organs remarkable for the activity of their metamorphoses (as, for instance, the muscles) contains far less phosphates than the corresponding blood returning from organs which exhibit a less amount of vital activity*; moreover careful analyses have proved that even in the plastic secretions from wounds there is a larger proportion of phosphates than in the corresponding liquor sanguinis (see p. 387). These facts seem to warrant the view that the presence of phosphates is necessary for the formation of cells and tissues, although they by no means entitle us to hold that plasticity is due to them alone.

Different forms of exudations.

(297.) In morbid anatomy we recognise (with Rokitansky) three leading forms of exudation, viz. — (1) fibrinous exudation, which is again divisible into the simple (or plastic), the croupous, and the tuberculous varieties; (2) albuminous exudation; and (3) purulent exudation.

* Lehmann's Physiological Chemistry, vol. iii. p. 137.

Chemical investigation has as yet only been satisfactorily made of fibrinous plastic exudations, and of purulent exudations or pus.

Fibrinous plastic exudation.

The fibrinous plastic exudation is the only one which can be easily obtained in a perfectly fresh and tolerably pure state. Fresh wounds afford the best means of procuring it, after the hæmorrhage has stopped; but it can be obtained in larger quantity from animals *, after portions of muscle have been cut away under the skin, and consequently from wounds with a loss of substance. A perfectly fresh exudation of this kind exhibits all the physical and chemical characters of the intercellular fluid of the blood. In the fluids of this kind examined by Lehmann †, he always found more water, less albumen, and more phosphates and potash-salts than in the corresponding liquor sanguinis. He could not determine the relative proportions of fibrin: in birds (his experiments were made on rabbits and geese) there was always rather more fat in the exudation than in the blood-plasma.

Recent exudations in the rare cases in which we obtain them from serous sacs in the human subject, present very different characters, being always separated into a coagulum and a fluid.

The coagulum varies very much in form and colour; its microscopical characters are principally those of spontaneously coagulated fibrin, but in addition to swollen and almost spherical blood-discs, it usually contains granules, nuclei, and occasionally cytoid corpuscles; it swells in water containing hydrochloric or acetic acid, but does not form a mass of such perfect translucence as the fibrin of the blood.

The fluid portion is generally clear and transparent, only becoming opalescent and turbid after the exudation has re-

* Birds, not being prone to suppuration, are the best animals to use. Frogs cannot be employed in consequence of the large quantity of lymph, which is poured out of their subcutaneous lymphatics, and vitiates the purity of the exudation.

† Physiological Chemistry, vol. iii. pp. 133 and 150.

mained for some time in the cavity. The reaction is commonly less alkaline than that of blood-serum. Albumen is precipitated from it on boiling, either in curd-like clots, or in a gelatinous mass, and the filtered fluid forms the so-called casein-membrane on its surface—an indication, however, in this case not of the presence of casein, but of an alkaline albuminate (see p. 106), for both the rennet-test and acetic acid here give negative results. The salts and extractive matters resemble those occurring in the blood. The quantitative composition of these exudations when compared with that of the corresponding blood, is by no means fixed. The relative quantities of fibrin cannot be determined. No definite ratio seems to exist between the part of the exudation which remains fluid, and the serum of the corresponding blood, but generally the solid residue of the fluid portion of the exudation is inconsiderable, and consequently there is a relative excess of water. There is usually less of the coagulable protein-substances, but rather more of extractive matter in the exudation-fluid than in the corresponding blood-serum. The collective salts are somewhat higher in the exudations than in the blood-serum, and on comparing the individual salts, we find without exception relatively and absolutely more phosphates and potash-salts in all the exudations that have been examined than in the blood-serum.

Passing without remark over the croupous, tuberculous, and albuminous forms of exudation, on which chemistry has as yet thrown no satisfactory light, we proceed to the consideration of the purulent exudation.

Pus.

(298.) The purulent exudation, or pus, occurs as a thick yellowish fluid, which differs from every other exudation by containing a large number of corpuscles, which are distributed through it with tolerable uniformity. Hence pus, like blood, consists of corpuscles and an intercellular fluid or serum.

Pus-corpuscles.

These corpuscles, which commonly range from 0·004 to 0·005 of a line in diameter, consist of a cell-membrane, which often

appears granular, of viscid transparent contents, and of a nucleus that adheres to the cell-wall, and therefore lies eccentrically. As no chemical or microscopical differences can be observed between these pus-corpuscles and the colourless blood-corpuscles, the lymph-corpuscles, and mucus-corpuscles, Henle has proposed to call them all by the common name of cytoid (or cell-like) corpuscles. See *Plate V. fig.* 8 (*a*).

Difficult as it is to separate the red corpuscles from the blood, it is still more difficult to separate these corpuscles from the surrounding intercellular fluid. No addition of any saline solution will here render the fluid capable of filtration. Like the blood-corpuscles, they possess a sinking tendency, but they sink so slowly, that the pus begins to become decomposed before the process is nearly accomplished.

Fermentation of pus.

Pus when exposed to the air, very soon begins to exhibit certain changes. It may undergo either acid or alkaline fermentation, the latter being equivalent to ordinary putrefaction. Acid pus is probably of very rare occurrence in the animal body (as far as I know, only having been met with in a few cases of empyema, and of phthisical sputa), and this is the more remarkable because pus rapidly loses its normal alkaline reaction when exposed, in a corked bottle containing air, to a summer temperature, and in the course of time becomes acid. It forms both volatile and fixed fatty acids: butyric acid can be chemically detected in it, and margaric acid is liberated from the pre-existing neutral fat which normally exists in pus, and may be readily detected by the microscope (see *Plate V. fig.* 8 *b*).* The acids which are thus generated act in the same manner as dilute acids do when added to fresh pus; that is to say, they render the cell-wall

* After pus has stood for some months, the different fats appear in the most beautiful forms, such as no artificial means are able to produce. Under the microscope we see confused masses of fine threads of margarin, and ensiform, or lily-leaf-shaped, variously contorted bundles of crystals of margaric acid, together with tablets of cholesterin.

transparent, and bring the previously concealed nuclei into view.

Pus, when mixed with mucus or blood, or when secreted on an unhealthy-looking surface, rapidly undergoes alkaline fermentation, without having previously become acid. It begins to evolve ammonia and hydrosulphate of ammonia; the cytoid corpuscles become destroyed or run together into a gelatinous mass; nuclei are no longer to be seen either isolated or in the corpuscles; and at length the only morphotic elements are molecular granules and vibriones.

The cytoid corpuscles are readily acted on by endosmotic currents; their diameter depending to a great extent on the specific gravity of the fluid in which they float; hence in saliva they are larger, and in blood they are smaller, than in purulent serum.

Since the intercellular fluid of pus doubtless bears a definite relation to the intercellular fluid of the blood, it obviously follows that in those diseases in which the specific gravity of the liquor sanguinis is altered, there will likewise be an alteration in the size of the pus-corpuscles. For if we dilute pus with distilled water, we observe that the corpuscles become much swollen, that the cell-membrane loses its granular character, and that the nucleus consequently is brought distinctly into view: some corpuscles even burst from the absorption of water.

Action of chemical reagents on the pus-corpuscles.

Very dilute mineral acids and moderately dilute organic acids, act similarly to water, and may be employed (acetic acid for instance) in bringing the nuclei into view. When the nucleus is originally visible, and of a simple lenticular form, it retains this appearance after the addition of acids, but in those cases in which it is originally invisible, or where its appearance can only be detected by a dark spot in the corpuscle, the nucleus is generally tripartite.

Solutions of neutral alkali-salts contract and shrivel the corpuscles by extracting their water: they lose their clearly

defined outline and are converted into minute granular jagged bodies; while the caustic alkalies rapidly destroy the corpuscles.

Pus-corpuscles are entirely destroyed by the addition of bile, or of solution of glycocholate, taurocholate or cholate of soda.*

As incidental morphotic constituents of pus, we often meet with fat-globules, blood-corpuscles, epithelium, granular or exudation cells, fragments of connective tissue, &c.

The serum of pus. The serum of pus is perfectly clear, colourless, or very faintly yellow, of a weak alkaline reaction, and coagulates on the application of heat into a dense white mass. Its principal constituent is albumen, which occurs in it in varying proportions, from 1·2 to 3·7%.

Certain modifications of the protein-bodies, known as mucin and pyin, are occasionally found in the pus-serum: casein, or a substance closely allied to it, chondrin, glutin, and leucine, have also been found.†

Pyin. The chemical characters of mucin have been already described (see p. 287). Pyin, which was discovered by Güterbock in pus, but which is by no means an invariable constituent of that fluid, may be described as a derivative from the protein-bodies, which is precipitated from its watery solution by acetic acid, but is perfectly insoluble in an excess of that acid, while hydrochloric and nitric acids only cause a slight turbidity, which disappears on the addition of an excess of the reagent. It is precipitated by alum, but not by ferrocyanide of potassium, from its hydrochloric-acid solution; neutral acetate of lead and corrosive sublimate likewise throw it down. It is not coagulated by heat. Mulder regards pyin as identical with a substance which he had previously obtained by the prolonged boiling of certain albuminates in water,

* Von Dusch, Beiträge zur Pathol. des Icterus, u. s. w. 1854, pp. 11—15.

† Bödeker in Zeits. f. rat. Med., New ser. vol. vii. p. 146, &c.

and which he afterwards discovered in the blood and in fluid exudations, and to which, from its composition, he had given the name of tritoxide of protein. Lehmann expresses the opinion that the substance referred to by Mulder as occurring in the blood and exudations more closely resembles the peptones (which are briefly alluded to in the remarks "On the Gastric Juice" in p. 161, and are more fully noticed in the chapter "On Digestion") than pyin, since it is not thrown down by acetic acid.

Fat.

The fat probably belongs more to the corpuscles than to the serum. The fatty matter extracted by ether consists not only of olein and margarin, but of oleic and margaric acids, and of cholesterin. The collective fats vary from 2 to 6% of the fluid pus, the cholesterin alone often reaching 1%.

Solid constituents.

The solid constituents of normal pus range from 14 to 16%. The solid residue contains 5 or 6% of mineral constituents, the soluble salts being to the insoluble in about the ratio of

Salts.

8 to 1. Of the soluble salts, the chief is chloride of sodium, which is three times as abundant as in the serum of the blood: the soluble phosphates in the ash range from 3 to 10%. The insoluble salts consist of the phosphates of lime and magnesia, with a little sulphate of lime and peroxide of iron.

In the pus as in all other exudations, we meet with bile-pigment, the resinous acids of the bile *, urea, and sugar, as incidental constituents.

* Lehmann states that one of his pupils found glycocholate and taurocholate of soda in pus from an abscess in the thigh of a patient with jaundice. The action of the bile, described by Von Dusch, seems not to have been noticed in this case.

# CHAPTER XVI.

## THE SOLID TISSUES OF THE BODY.

### SECTION I. — THE OSSEOUS TISSUE.

The osseous system.

(299.) The bones are the most indestructible of all the parts of the animal organism; human and animal bones at least 3000 years old, discovered in Egyptian tombs, being found to present the same composition as perfectly recent bones; and even fossil bones of extinct animals scarcely differ in any important point from the normal type.

Composed of organic and inorganic matters.

Bone consists chemically of animal and earthy or inorganic matters.

The external surface of bone is covered by periosteum (a membrane provided with nerves and vessels), which, as well as the cartilaginous portion, can be converted by boiling into gelatin. If a bone is suspended in dilute hydrochloric acid at a low temperature, all the earthy matter becomes gradually dissolved, and the mere cartilage remains, retaining the precise form of the original bone. It is supple, transparent, and soft; but, on drying, it becomes of a darker colour, hard, and somewhat shrivelled, and when boiled becomes rapidly converted into gelatin, leaving the vessels, &c., unacted on. When bone is submitted to thorough incineration, all the organic portion is destroyed, and nothing remains but the earthy matter mixed with certain salts, which have been formed during the process of incineration (such as carbonates of the alkalies), and with free lime, formed by the expulsion of the carbonic acid from carbonate of lime. These two simple experiments suffice to show that both organic or animal,

and inorganic or earthy constituents enter largely into the composition of bone.

In addition to cartilage, which forms the great mass of the animal matter, the bones of all the vertebrata are found to contain fat (which occurs in very varying quantities) and albuminoid matter, which is not convertible into gelatin, and which seems to be derived partly from the blood-vessels, and partly from the membranous structure which has been proved by histologists to line the minute cavities commonly known as bone-corpuscles. The inorganic constituents of bones, which usually form considerably more than half the mass, are mixed in various proportions, and consist of phosphate of lime ($3CaO.PO_5$), which is always the preponderating ingredient, of carbonate of lime, and of a little fluoride of calcium and phosphate of magnesia. The discovery by Von Bibra that the bone-ash of reptiles and fishes (see p. 137) contain soluble sulphates, is deserving of special notice, because, as a general rule, the bone-ashes of most animals do not contain a larger amount of soluble salts (chloride of sodium and carbonate of soda) than might be referred to the juices permeating the bones.

Bone-cartilage or ossein.

The bone-cartilage or ossein (as certain recent writers term it) is obtained in the manner we have already described by means of dilute hydrochloric (or nitric) acid. If the action of the acid has been continued for a sufficiently long time, the ossein yields on incineration a mere trace of ash, and its atomic composition has been found to be precisely identical with that of the glutin which is derived from it by boiling. Frémy* has shown that the ossein of mammals, birds, amphibians, reptiles, and fishes is identical, and that the age of the individual has no effect on its composition. It is found, however, that in the embryo, even up to the latest period of intra-uterine life, the bones yield no glutin, and,

* Ann. de Chim. ch. de Phys., 3 sér. vol. xliii. pp. 47—107.

therefore, must contain a substance differing essentially from ossein. It appears from the investigations of Von Bibra* and Ragsky† that the character of the ossein is not affected by disease of the bone.

In the bones of certain water-birds and fishes Frémy found a substance which, although isomeric with ossein, differed from it in not yielding gelatin on boiling; and which, when treated with hydrochloric acid, yielded a white, transparent, elastic substance.

The fat which occurs in the analysis of well-macerated bones is for the most part due to the presence of marrow, &c.; very little fat (olein) exists in the true osseous tissue.

The organic matters occurring in bone range from 30 to 40%, about 33% being the average in the human subject.

Analyses of different bones of the body.

The following analyses by Von Bibra of different bones from the body of a man aged twenty-five or thirty years, will serve at the same time to give a general idea of the chemistry of bone, and to show how the composition of the different bones varies in the same subject: —

| | Femur. | Tibia. | Humerus. | Ulna. | Os occipitis. | Costa. |
|---|---|---|---|---|---|---|
| Phosphate of lime with a little fluoride of calcium | 59·63 | 58·95 | 59·87 | 59·30 | 58·43 | 55·66 |
| Carbonate of lime . . | 7·33 | 7·08 | 7·76 | 7·35 | 8·00 | 6·64 |
| Phosphate of magnesia . | 1·32 | 1·30 | 1·09 | 1·35 | 1·40 | 1·07 |
| Soluble salts . . . | 0·69 | 0·70 | 0·72 | 6·73 | 0·90 | 0·62 |
| Cartilage . . . . | 29·70 | 30·42 | 29·28 | 29·98 | 29·92 | 33·97 |
| Fat . . . . . | 1·33 | 1·55 | 1·28 | 1·29 | 1·35 | 2·04 |

In his different analyses of human bone Von Bibra found the phosphate of lime with fluoride of calcium to range from 63·17 to 42·32, the carbonate of lime from 10·9 to 4·46, and the phosphate of magnesia from 1·72 to 11·89%.

Lehmann gives the following numbers as representing the average composition of the mineral constituents in 100 parts of bone: — 57 parts of phosphate of lime, 8 of carbonate

* Chem. Untersuch. über die Knochen u. Zähne, 1844.

† Quoted in Rokitansky's Morbid Anatomy.

of lime, 1 of fluoride of calcium, and from 1 to 2 of phosphate of magnesia.

From the analyses of different bones of the same person, it appears that the bones of the extremities are richer in mineral constituents than those of the body (the vertebræ, os innominatum, ribs, &c.), and that the femur and humerus are more earthy than the other long bones; that the cranial bones closely resemble the latter in this respect, while the metacarpal and metatarsal bones resemble those of the trunk. The spongy bones contain rather more organic matter than the others; the short bones contain the most fat, and the flat bones the most water.

Bones at different ages.

Neither age nor sex seems to impress any special character on the composition of bone. In the following table all the analyses are by Von Bibra, and the selected bone is the femur. We give only the most important constituents — viz., phosphate of lime, including fluoride of calcium, carbonate of lime, and cartilage.

| | Child 9 months. | Child 5 years. | Woman 25 years. | Man 58 years. | Woman 78 years. |
|---|---|---|---|---|---|
| Phosphate of lime | 48·1 | 60·0 | 57·4 | 58·2 | 57·4 |
| Carbonate of lime | 6·1 | 5·9 | 8·9 | 8·4 | 7·5 |
| Cartilage | 41·7 | 31·3 | 29·5 | 31·4 | 32·1 |

Bones of mammals generally,

The researches of Von Bibra and Frémy on the bones of mammals show that a larger amount of carbonate of lime occurs in the bones of herbivorous than in those of carnivorous animals, and that the bones of pachyderms and cetaceans are especially rich in this constituent. (In the spongy substance of the femur of a horse Von Bibra found 18·9% of carbonate of

of birds,

lime.) They likewise show that the bones of birds contain relatively more earthy matters than those of mammals (sometimes, as in the Rasores, amounting to 76 or even 84%); that in birds the ratio in which the carbonate of lime stands to the phosphate, is higher than in mammals; that the bones of granivorous birds always contain a little silica, and that birds' bones contain more fat than those of mammals.

The bones of amphibians, reptiles, and fishes, are comparatively poor in mineral constituents, and their ash always contains sulphate of soda. Fishes' bones are richer in fat and in water than any other bones. of reptiles and fishes.

In almost all diseased bones we find a diminution of the mineral constituents, and often an excess of fat. Analysis has not done much to elucidate the nature of the various morbid processes occurring in bone, and it will suffice if I direct the reader's attention to the fact that he will find the most trustworthy results on this subject collected in the second volume of Simon's "Animal Chemistry," pp. 406—413. Morbid bones.

## SECTION II. — THE TEETH.

(300.) The teeth are composed of dentine, enamel, and cement. The teeth.

The chemical composition of dentine is very similar to that of bone; the quantitative ratio between the organic and inorganic constituents approximating very closely to that occuring in the denser bones, and averaging 28 : 72. From 3 to 8% of carbonate of lime has been found with from 65 to 67% of phosphate of lime, together with a little fluoride of calcium and phosphate of magnesia. Dentine.

The enamel yields no cartilage, and often contains not more than 2% of organic matter (apparently membranous tissue). In the enamel of human teeth, Berzelius found Enamel.

| | |
|---|---|
| Phosphate of lime with fluoride of calcium . | 88·5 |
| Carbonate of lime . . . . | 8·0 |
| Phosphate of magnesia . . . | 1·5 |
| Membrane, alkali, and water . . | 2·0 |

Nearly similar results have been obtained by Von Bibra and Frémy. The former chemist found as much as 4% of fluoride of calcium in the enamel.

Cement. The cement has been very imperfectly examined, but it seems to be chemically almost identical with bone.

The researches of Lassaigne and Von Bibra on the teeth of different animals, have yielded no very important results. No definite difference could be detected between the teeth of herbivorous and carnivorous animals.

Carious teeth. According to Marchard, carious teeth contain an excess of carbonate of lime.

## SECTION III. — CARTILAGE.

(301.) We must distinguish between true cartilage and fibro-cartilage.

True cartilage. True cartilage consists of a uniform-looking matrix which presents numerous small cavities containing nucleated cells. On closer (microscopic) examination, the matrix is however seen to be either granular or fibrous. In either case, on boiling the cartilage in water for a prolonged period (from 12 to 48 hours, according to its solubility), or on exposing it to the action of a Papin's digester for one hour, everything dissolves excepting the cells. Hence it is only the matrix or intercellular substance which yields chondrin; the chemical composition of the cartilage-cells being obviously different from that of the structure in which they are embedded.

Fibro-cartilage. Fibro-cartilage presents a more decidedly fibrous matrix than true cartilage, the cells having apparently the same structure in both varieties. The gelatin yielded by this fibrous intercellular substance is, however, not identical with the chondrin obtained from true cartilage, for its solution is only slightly precipitated by tannin, and the alum-precipitate, although abundant and compact, does not redissolve in an excess of the test.

No very accurate quantitative analyses of cartilage have been made. Dried cartilage yields from 2 to 5% of fat, which

seems to be chiefly deposited in the cells. In fresh cartilage the water ranges from 54 to 70%. The costal cartilages contain from 3 to 6% of mineral constituents, consisting of the phosphates of lime and magnesia, chloride of sodium, carbonate of soda, and sulphates yielded by the organic matters in the process of incineration.

## SECTION IV. — THE HORNY TISSUES.

(302.) Under the term horny tissue, we include epidermis, nails, claws, hoofs, horns, whalebone, tortoiseshell, hair, wool, &c. Horny tissues.

These substances are much more interesting in their histo-chemical, than in their general chemical relations; and we shall only notice a few isolated points on which chemistry has thrown some light.

The following table shows the elementary composition of several of the substances belonging to this group, after being boiled in water, alcohol, and ether. Their ultimate composition.

| | Epidermis from sole of foot. (Mulder.) | Nails. (Mulder.) | Horses' Hoof. (Mulder.) | Cows' Horn. (Tilanus.) | Hair. (Laer.) | Wool. (Scherer.) |
|---|---|---|---|---|---|---|
| Carbon . | 50·28 | 51·00 | 51·41 | 51·03 | 50·65 | 50·65 |
| Hydrogen . | 6·76 | 6·94 | 6·96 | 6·80 | 6·36 | 7·03 |
| Nitrogen . | 17·21 | 17·51 | 17·46 | 16·24 | 17·14 | 17·71 |
| Oxygen . | 25·01 | 21·75 | 19·49 | 22·51 | 20·85 | 24·61 |
| Sulphur . | 0·74 | 2·80 | 4·23 | 3·42 | 5·00 | |

By prolonged boiling (for several days) in sulphuric acid, most of these substances yield tyrosine and leucine (see pp. 32, 34).

Von Bibra has determined the percentage of sulphur in a number of the substances of this class. In cows' horn he found 3·04, in the hoof of the deer 3·02, in the claw of the dog 2·7, in human nails 2·73, in whalebone 3·49, and in human hair, as the mean of 46 determinations, 4·83 (the extremes being 3·92 and 8·23).

Laer, who has carefully studied the chemistry of the hair, The hair.

was unable to obtain any special pigment from it, but the microscope revealed the presence of pigment-granules in the cortical substance. He ascribes the whiteness of the hair of aged persons to the presence of air in it. The view maintained by Vauquelin, that the colour of the hair is influenced by the amount of iron which it contains, seems to be without foundation.

The quantity of fat extracted by Von Bibra from the hair of men and animals varied from 0·023 to 4·43%. In this fat Laer found only margarin, olein, and margaric acid, but Von Bibra also discovered cerebric acid. In cows' horn he found 2·1, and in the cast-off skin of a snake 7% of fat.

The inorganic matters in this class of tissues scarcely average 1%. Epidermis yields from 1 to 1·5, the nails 1, whalebone 1·1, tortoiseshell 0·5, hair from 0·3 to 2 in man (although more than 4 in certain animals), wool from 0·8 to 2, and feathers from 0·7 to 1·8%.

According to Von Bibra the ash yielded by hoofs contains much sulphate of lime and sulphate of magnesia, smaller quantities of silica and earthy phosphates, traces of chlorine and iron, and no carbonic acid. The hair both of men and animals contains the same substances, with traces of carbonates and fluorides. The silica in human hair amounts to about 0·2%; in feathers it is much more abundant, sometimes forming one half of the ash.

Glycogen in the horny tissues in fœtal life.

Bernard has recently discovered that (in many animals), during the first half of intra-uterine life, glycogen occurs in those cells which form, or precede the formation of, the horny tissues, as, for instance, the epithelium and epidermis, the hoofs, claws, and incipient horns.

As most of our knowledge of this substance, glycogen, has been obtained since the portion of this volume, treating of the sugars, was printed (1857), I shall here introduce a brief notice of it.

Composition and

Glycogen was discovered in the liver by Bernard, and has

been analysed by Pelouze, who assigns to it the formula $C_{12}H_{11}O_{11}.HO$. Its properties seem to indicate that it should be placed between starch and dextrine. In contact with saliva, pancreatic juice, or diastase, it becomes rapidly converted into sugar; and the presence of blood or of the parenchyma of the liver induces the same change in it. It occurs as an amorphous matter in the hepatic cells. During fœtal life, before the liver begins to discharge its proper functions, it is, however, not found in that organ; but it has then been found by Bernard, in special cells in the placenta (in the rodents) or in aggregations of cells distributed over the amnion, also in the fœtal muscles, lungs, &c. In severe forms of disease, and especially in febrile affections, it seems to be temporarily absent from the liver.

properties of glycogen.

## SECTION V. — MUSCULAR TISSUE.

(303.) Muscular tissue, whether smooth or striated, being made up of different morphotic elements which it is impossible to separate, is not well adapted for ordinary chemical investigation, although micro-chemical or histo-chemical researches have thrown much light on its nature and composition.

Muscular tissue.

We begin with the consideration of smooth muscle, which consists mainly of nucleated contractile fibre-cells, grouped together in bundles and layers, and permeated by a muscular juice; no sarcolemma being detectible.

Smooth muscle.

The substance of which the cells are composed is soluble in very dilute hydrochloric acid (1 to 1000), and on neutralising the acid solution we have at first a hardly perceptible jelly, which after a time collects in flakes at the bottom of the vessel. These flakes are soluble in lime-water, and on the application of heat the solution coagulates as if it contained albumen; they likewise dissolve readily in alkalies and very dilute acids, but not in solution of carbonate of potash or in

water. Hence (see p. 112) this substance is perfectly identical with the syntonin or fibrin of striped muscle.

The juice or fluid permeating the smooth muscular tissue approximates much more closely in its chemical characters to the corresponding fluid which moistens the striped tissue, than to the blood-plasma or any other fluid. It is, however, usually neutral or even faintly alkaline * in its reaction, whereas the ordinary juice of striped muscle is acid; in addition to albumen it contains more or less casein †, creatine, hypoxanthine, very small quantities of lactic, butyric, acetic, and formic acids, and a relative but not an actual excess of the potash over the soda compounds.‡

The muscular tissue of the Mollusca is of the smooth or unstriped variety. Valencienres and Frémy have recently examined the flesh of acephalous molluscs, and cephalopods, and have found that in addition to creatine and creatinine, it contains considerable quantities of taurine (see p. 53), and of super-phosphate of lime, which latter substance imparts to the tissue an acid reaction; they likewise detected oleophosphoric acid in small quantity.

Striped muscle.

On examining the primary bundles of striated muscular fibre after the removal (as far as possible) of all extraneous tissues, we find that it presents three morphotic elements, which, as micro-chemical investigations show us, are altogether distinct from one another in composition, namely, the fibrils, the nuclei, and the sarcolemma.

The substance forming the fibrils contained within the

* This statement is not universally true. Lehmann found that the juice from the muscular coat of the stomach of the pig was distinctly acid, although less so than that derived from striped muscle; and the corresponding fluid from the middle arterial coat of the ox was found by the same chemist to be acid, although Schultze had described it as alkaline.

† Schultze found no less than 7·24% of casein in the well dried muscular coat of the aorta. Ann. d. Chem. u. Pharm. vol. lxxi. pp. 277—293.

‡ The ratio of the potash to the soda was as 38 : 62 in the juice from the muscular coat of the pig's stomach, and as 42 : 58 in that of the middle coat of the arteries.

sheaths of sarcolemma is the most important constituent. It seems to be identical with the syntonin described in p. 112, for on treating well-prepared muscular fibre, either on a comparatively large scale, or under the microscope, with a dilute solution of hydrochloric acid (1 part to 1000), we observe that the sarcolemma-tubes gradually discharge their contents, after which syntonin is found in the solution. We must, however, recollect that, as we obtain this substance for the purpose of analysis, it is in a coagulated state, while during life, or as long as muscle retains its characteristic irritability, it exists within the sarcolemma in a soluble form; and we have no means of ascertaining what changes albuminous bodies of this kind undergo in the process of coagulation. In the coagulation of globulin and of hæmatocrystallin an acid seems to be separated (see p. 217) when either of these substances is coagulated by boiling; and Kühne, in watching the soluble syntonin escaping from the sarcolemma-tubes of frogs' muscles, thought that he saw indications of the presence of a free acid during its spontaneous coagulation. Hence the fibril-substance, on which histo-chemical observations are made in the syntonin which we submit to analysis, is probably a mere derivative or product of decomposition of the preponderating substance in living muscle.

Substance forming the fibrils.

Various histo-chemical reactions presented by the sarcolemma, and its incapacity of being converted by boiling into gelatin, indicate that it is not allied to connective tissue; its elasticity, which is unaffected by the action of either acids or alkalies, seems to connect it with elastic tissue. The granules which are brought to view in the sarcolemma when it is emptied of its contents by the action of acids or alkalies consist chiefly of fat.

The chemical nature of the nuclei, which are embedded in the sarcolemma, has not been clearly made out; but they seem in many respects to resemble, although they are not identical with, the substance of the fibrils.

Substance of the nuclei.

The muscular juice.

The fluid which permeates and surrounds the various morphotic elements, the muscular juice, next claims our attention. This juice, when we express it from the muscular tissues of men or animals after their death, is almost always acid. The

Its reaction.

cause of this acidity was maintained long ago by Berzelius to be lactic acid, while Liebig subsequently showed in his admirable "Researches on the Chemistry of Food," that the acidity is due to the simultaneous presence of lactic acid and acid phosphate of lime. Subsequent observers (Von Bibra and Enderlin) have found the intensity of the reaction variable, and have even observed that in perfectly fresh flesh the reaction is sometimes neutral. Du Bois Reymond has just (1859) shown, by a series of most carefully conducted experiments, that fresh or living muscles (muscles still sensitive to galvanic stimulus) do not exhibit an acid reaction, but rather tend to alkalinity. He has further shown that the acid reaction only ensues with the commencement of the *rigor mortis* or the coagulation of the syntonin. This view is in strict accordance with the facts previously observed by Kühne, to which we have already adverted. Hence it would appear that there is an intimate connection between the acid reaction and the coagulation of the syntonin. There are, however, as Du Bois Reymond subsequently discovered, certain conditions under which perfect coagulation of the syntonin may occur without the development of free acid in the muscles. For by a comparatively high degree of heat, by concentrated solutions of chloride of sodium, or sulphate, or nitrate of potash, or by the action of alcohol, the syntonin may be coagulated in the living (that is to say, the fresh and still irritable) muscle, without the development of an acid reaction; the muscle under these conditions presenting a neutral or faintly alkaline reaction. The occurrence of the acid reaction is further shown to be perfectly independent of the access of atmospheric air.

Although the *rigor mortis* is the ordinary condition that

leads to the development of free acid by the syntonin, there are other ways and modes by which it may liberate a free acid; for Du Bois Reymond has convinced himself, by a series of experiments on frogs, rabbits, and dogs, of the fact noticed many years ago by Berzelius, that the acidity is increased in muscles that had been previously strongly exercised; and that during life the muscles may temporarily attain an acid reaction, as a consequence of often-repeated contractions, which disappears after sufficient rest, when they return to their normal neutral, or faintly alkaline reaction. Muscles, which like the heart are in a state of perpetual activity, are not always found to exhibit an acid reaction, but the free acid is developed in them earlier than in other muscles.

We must regard it then as an established fact that the muscles, in the exercise of their normal functions, develop a free acid, but we are not in a position to affirm with certainty that this acid is identical with the lactic acid which is yielded by dead muscular tissue. Valenciennes and Frémy refer the acid reaction of muscular juice to acid phosphate of potash, but this view is opposed by the fact (quoted by Du Bois Reymond) that this salt has only a transitory action on litmus paper, while the muscular juice permanently reddens it.* There is no doubt that muscles which have become rigid after death, contain a considerable quantity of free lactic acid; but since all this lactic acid is not formed (or, at all events, does not appear) instantaneously, the phosphate of potash may be converted, by its gradual agency, into an acid salt.

Muscular contraction dependent on the presence of oxygen.

It was first proved by G. von Liebig that muscle is dependent on oxygen to enable it to contract. He found that frogs' muscles retained their contractility much longer in an atmosphere of oxygen than in one which did not contain that

* In the case of perfectly fresh bullock's heart, it has however been observed that, whatever may be the cause of the acid reaction, the reddening of the litmus paper soon disappears.

substance; and he further showed that while a muscle is in a state of contraction oxygen is absorbed, and a corresponding quantity of carbonic acid is exhaled, facts which confirm the view that a large portion of the carbonic acid formed in the animal body is generated, not in the capillaries, but in the parenchyma of the organs, and is especially produced by muscular action. Subsequent experiments, made independently by Matteucci and Valentin, show that the quantities of absorbed oxygen and exhaled carbonic acid are proportional to the contractions.

It has long been known that heat is liberated in muscles by the act of contraction; recent observations of Helmholz and others show that this phenomenon may be observed even in muscles from which the flow of blood has been cut off.

It has been further observed that the muscles of animals that have been hunted to death, the muscles of men or animals in whom death has been preceded by severe convulsions, as well as muscles whose energy has been exhausted by repeated galvanic stimulation, become putrid much sooner than muscles which were in a state of repose previously to death. Muscles which during life have been thrown into tetanic spasm, either by disease or by strychnine, become rigid almost immediately after death, or in other words the syntonin at once coagulates in them.

Physical and chemical characters of the muscular juice.

The muscular juice, as we obtain it for the purpose of examination, even if derived as rapidly as possible from the flesh of recently killed animals, must obviously differ considerably from the fluid permeating the tissues during life. It occurs as a whitish or opalescent fluid of a more or less acid reaction, and contains albumen, creatine, creatinine, hypoxanthine, inosite *, lactic acid, inosic acid, and several volatile acids, as

* I hardly know whether inosite should be regarded as an ordinary constituent of the muscular juice. Scherer (see p. 92) originally obtained it from the heart of the ox, and it has been unsuccessfully sought for by Socoloff and Panum (in Scherer's Laboratory) in the juice of other muscles. Lehmann, however, states without giving his authority, that it is present in smaller quan-

formic, acetic, and butyric acids; it is probable, however, that these volatile acids are the result of incipient decomposition. Traces of uric acid have also been found in the muscular tissue, but the most careful investigations have failed in detecting the slightest indication of urea in the juice of healthy muscular tissue, although it is found there in cases of uræmia.* We do not know whether the muscles possess any special pigment. Fat is always present, even after the most careful removal of all visible traces of it. In addition to the neutral fats, Valenciennes and Frémy maintain that this tissue contains oleo-phosphoric acid. Böttcher found from 1·5 to 1·9% of fat in the muscular tissue of the human heart (or from 8 to 10% in the dried tissue), and Von Bibra found from 10 to 15% of fat in the dried muscle of the human thigh.

Muscles on being boiled yield from 2 to 6% of gelatin, which arises from the connective tissue which holds together the primitive bundles.

The soluble matters which can be extracted from muscular tissue range from 6 to 8%.

With regard to the mineral constituents the potash-salts and phosphates preponderate over the soda-salts and chlorides, and the phosphate of magnesia amounts to about double the phosphate of lime.

The amount of syntonin in the muscles is very variable; it appears to be more abundant in the muscles of old than of young animals.

tities in the other muscles. The unripe fruit of *Phaseolus vulgaris*, a kind of bean, has been found by Voit to contain inosite — a fact of interest, as an additional illustration of the frequent identity of animal and vegetable products. Scyllite, a substance which in most of its properties closely resembles inosite, has recently been discovered by Frerich's and Städeler in the muscles and other tissues of the Plageostomata, an order of cartilaginous fishes including the sharks, rays, &c. Journ. f. pr. Chem. vol. lxxiii. pp. 48—55.

* Small quantities of urea have been found in these cases by Buhl and Voit (Zeits. f. rat. Med. New Ser. vol. vi. p. 94), and by Von Bibra (Ann. d. Chem. u. Pharm. vol. xciv. pp. 206—215). Strangely enough Frerichs and Städeler report that the muscles of the Plageostomata contain a considerable quantity of urea, while the flesh of other fishes does not yield a trace.

The quantity of water in the muscles has been determined by several chemists. Fresh muscular tissue from the ox yielded 77·6% of water (Schlossberger), while human muscles yielded from 72·6 to 74·5% (Von Bibra), and the human heart from 81 to 82% (Böttcher). The quantity of water in the muscles of persons who have died from cholera is considerably diminished and has been found as low as 69·1%.

The following table, drawn up by Lehmann, represents the average composition of the muscular tissue of the ox: —

Composition of muscular tissue.

| | | |
|---|---|---|
| Water | 74·0 | 80·0 |
| Solid constituents | 26·0 | 20·0 |
| Muscular fibre (syntonin) | 15·4 | 17·7 |
| Gelatigenous substance | 0·6 | 1·9 |
| Albumen | 2·2 | 3·0 |
| Creatine, Creatinine, Hypoxanthine, Inosite, Inosic acid | Too small to be determined. | |
| Fat | 1·50 | 2·30 |
| Lactic acid ($C_6H_5O_5.HO$) | 0·60 | 0·68 |
| Phosphoric acid | 0·66 | 0·70 |
| Potash | 0·50 | 0·54 |
| Soda | 0·07 | 0·09 |
| Chloride of sodium | 0·04 | 0·09 |
| Zinc | 0·02 | 0·03 |
| Magnesia | 0·04 | 0·05 |

Glycogen in fœtal muscle.

Bernard has recently found glycogen in the muscles of the various animals in the embryonic state. (Its result, sugar, he had discovered in these organs some years previously. See p. 90.) It is scattered over the sarcolemma-tubes in the form of granules; and may be found during the whole of intra-uterine life, disappearing a few hours (6 to 24) after birth.

## SECTION VI. — THE BRAIN AND NERVOUS TISSUE.

Nervous tissue.

(304.) The various morphological elements entering into the composition of nervous tissue, present many points of difference in their chemical composition.

Its morphotic elements.

The investing membrane of the nerve-fibres shows by its micro-chemical reactions, that it does not consist of areolar or connective tissue; it seems to be allied to, though not identical with, the protein-bodies.

The axis-cylinder consists of a protein-substance closely allied to syntonin.

The medullary matter most probably consists of a soluble protein-body and a dissolved fat. The addition of water brings this substance into view, and is said to coagulate it, but the appearance which is thus produced is more likely to be caused by a separation of fat, than by the coagulation of a protein-body.

Our knowledge of the constituents of the nerve-cells is very imperfect. The cell-walls are slightly soluble in acetic acid, and insoluble in carbonate of potash, and so far resemble syntonin; and the contents of the cells appear to consist partly of a dissolved, and partly of an only swollen protein-substance, together with a little fat.

The analysis of the collective nervous tissue (for it is impossible to separate the different morphotic constituents), shows that it contains the following ingredients.

Composition of the brain.

Besides albumen coagulable by heat, Von Bibra found in the water-extract of the brain, various modifications of albuminous substances, which were not precipitated from their solutions by boiling; and at least two nitrogenous substances, one of which was soluble in water alone, and the other in water and alcohol.

Although several elaborate treatises have been published on the brain-fats, our knowledge regarding them is still some-

what vague. Boiling alcohol and ether extract a number of distinct substances, but it is questionable how far they are all entitled to be termed fats. Amongst the fatty matters detected by Frémy in the brain, may be mentioned olein, oleic and margaric acids, cerebric and oleo-phosphoric acids, and cholesterin. Von Bibra maintains that the brain-fats consist of cerebric acid and cholesterin, and of a series of fatty acids possessing different properties and different fusing points; these fatty acids not even being the same in different brains of one and the same species, and (as he conceives), undergoing perpetual decomposition in the living organism, passing into one another, and taking a share in the cerebral functions.*

* As the composition and very existence of several of the so-called fats of the brain are doubtful, I think it better to notice them briefly in a note, in preference to introducing them into the text.

The cerebric acid of Frémy seems to be very nearly, if not quite, identical with the cerebrin of Gobley, and the cerebrote of Couerbe. It is a white crystalline powder readily soluble in boiling, but almost insoluble in cold ether. It is insoluble in cold, but is tolerably soluble in boiling alcohol. Its most remarkable property is, that like starch it swells, but does not dissolve in boiling water.

The following analyses prove not only the identity of cerebric acid and cerebrin, but also the great similarity between this brain-fat and glycocholic acid, a similarity which has led Schlossberger to the idea (see p. 176), that the latter is the originator of the former.

| | Cerebric acid. Frémy. | Cerebrin. Gobley. | Glycocholic acid. Strecker. |
|---|---|---|---|
| Carbon . . . . | 66·8 | 66·8 | 67·1 |
| Hydrogen . . . . | 10·6 | 10·8 | 9·3 |
| Nitrogen . . . . | 2·4 | 2·9 | 2·9 |
| Oxygen . . . . | 19·3 | 19·6 | 20·6 |
| Phosphorus . . . . | 0·9 | 0·4 | |

Oleo-phosphoric acid (apparently the same substance as the eléencephole of Couerbe), is described by Frémy as a yellow thick fluid like olein, insoluble in water, but swelling a little in hot water (probably from a little retained cerebric acid). It dissolves in ether and in hot alcohol; and saponifies readily with the alkalies and with other bases, forming insoluble salts. When boiled for a long time with water or alcohol, it breaks up into olein and phosphoric acid — a separation that takes place much more quickly if a little mineral acid be added.

Gobley's investigations tend to show that very analogous, if not identical, substances occur in the yelk of egg, and in the brain. In both of them he finds a "matière visqueuse" consisting of cholesterin, lecithin, and cerebrin, together with other fats.

In addition to the fats, W. Müller, who has carefully analysed the brain both of man and the ox, mentions the following organic constituents of this tissue: creatine in small quantity (in the human brain, but not in the brain of the ox), a substance very similar to leucine (in the brain of the ox, but not in that of man), lactic acid in considerable quantity, inosite, a very little uric acid (in the brain of the ox), and certain volatile acids, as acetic and formic acids.

Succinic acid, glycine, creatinine, urea, cystine and taurine were sought for by Müller in vain.

The mineral constituents of the human brain were found by Breed to amount to 0·027% of the whole mass, and were composed of

The mineral constituents of the human brain.

| | |
|---|---|
| Phosphate of potash | 55·24 |
| Phosphate of soda | 22·93 |
| Phosphate of iron | 1·23 |
| Phosphate of lime | 1·62 |
| Phosphate of magnesia | 3·40 |
| Chloride of sodium | 4·74 |
| Sulphate of potash | 1·64 |
| Free phosphoric acid | 9·15 |
| Silica | 0·42 |

According to Schlossberger, the ash of the grey matter has a strongly alkaline, and that of the white a strongly acid reaction.

The amount of water varies in different parts of the brain; the white portions being considerably poorer in water, and richer in fat than the grey matter: indeed the water and

His lecithin is a neutral, uncrystallisable, viscid substance, which under the influence of acids or alkalies, breaks up into olein, margaric, and glycero-phosphoric acids.

For further information on these questionable substances, I may refer to Von Bibra's Vergleichende Untersuchungen über das Gehirn u. s. w., and to Schlossberger's Erster Versuch einer allgemeinen und vergleichenden Thier-chemie; II. Abtheilung: Das Nervengewebe.

the fat in the different parts of the brain seem to stand in an inverse ratio to one another; thus the cortical substance of the hemispheres contains from 84 to 88% of water and from 4·8 to 6·5% of fat, while the white substance of the corpus callosum contains only from 63 to 70% of water, and from 15 to 21% of fat.

The brain in the embryo, and in the young child, contains more water than the brain in adult life; and in old age the quantity of water seems to be slightly augmented.

One peculiarity of the brain-fat is the large quantity of phosphorus which it contains. The brain-fat even of the same brain contains varying quantities of phosphorus, according to the part from which it is extracted. Von Bibra found, in the case of a man aged fifty-nine, that the fat from the medulla oblongata contained 1·65, that of the cerebellum 1·83, and that of the optic thalami 1·54% of phosphorus, the mean for all the parts being 1·68%. From numerous observations, Von Bibra concludes (1) that the amount of phosphorus in the brain-fat is very nearly the same in man, in other mammals, and in birds; (2) that the phosphorus in the brain-fat of insane persons does not deviate from the mean amount; and (3) that extreme old age does not modify the quantity.

Action of chemical reagents on the nerves.

Some curious and interesting experiments have recently been made (by Ecker, Kühne, Birkner, and others), on the stimulation of the nervous action by chemical reagents. Motor nerves excite contractions in the muscles to which they are distributed when stimulated by dilute caustic alkalies (just as is the case with muscular fibre itself); muscular contractions are also excited by touching the motor nerves with mineral and organic acids, alkaline chlorides, glycerine, and tannates of the alkalies; but the solutions of these substances must be much more concentrated than would be necessary to cause muscular contraction if applied directly to muscle. On the other hand chromic acid, sulphate of copper, neutral

and basic acetate of lead, lime-water, and ammonia, which act energetically on muscular fibre, exert no influence in stimulating the nerves; while alcohol and creosote which excite no action on the muscles, act energetically on the nerves. It is, moreover, a remarkable fact, that curare or woorali poison, and coneine, completely deaden the nerves to any electrical or chemical stimuli, while the irritability of muscular fibre remains unaffected by these reagents. Birkner* has recently shown that many morbid conditions are induced by an excess or deficiency of water on the nerves.

## SECTION VII. — THE GLANDS AND THEIR JUICES.

Chemical constituents of the glands.

(305.) During the last few years, the glands and their expressed juices have been submitted to careful chemical analysis by Gorup-Besanez, Cloetta, and others. We shall briefly state a few of the chief results.

Gorup-Besanez found leucine in the pancreas, spleen, thymus gland, thyroid body, and (in small quantity) in the liver of the ox. In both the pancreas and the spleen, he also found a substance homologous to leucine (see p. 33). He failed in detecting tyrosine in the thymus, thyroid, liver, kidneys, lungs, and spleen, but once found a little in the pancreas. He found hypoxanthine (in very small quantity) in the spleen, thymus, and thyroid; and uric acid only in the spleen.

Formic (see p. 11), acetic (see p. 11), succinic (see p. 16), and lactic acids (see p. 22), were obtained from these glands.

Both Gorup-Besanez and Cloetta have found inosite in the spleen, liver, kidneys, thymus, pancreas, and lungs.

Cloetta has found cystine in some cases, and taurine in others, in the kidneys, and uric acid in the liver of the ox.

Scherer has found guanine in the pancreas of the ox.

* Das Wasser der Nerven in Physiologischer und Pathologischer Beziehung. 1858.

The inorganic constituents of the liver, spleen, and certain other glands have been carefully studied by Oidtmann in men and women of various ages, and in several of the lower animals. The following are some of his most important results.

1. The amount of ash usually increases with the age of the individual, while the amount of water decreases with the age.

2. In the liver the potash-salts preponderate over the soda-salts, whereas in the spleen the latter preponderate.

3. Chlorine is present in only small quantity in the liver and spleen, forming 2·5% of the ash in the former, and only 0·3% in the latter.

4. The quantity of phosphoric acid is large in the liver (43·37% of the ash) as compared with the spleen (18 to 27% of the ash).

5. The quantity of lime is not great in either the liver or the spleen, forming about 3% of the ash in the former, and 7% in the latter; while the magnesia does not average more than 1%.

6. In the spleen the iron is abundant, ranging from 7 to 16% of the ash; in the liver it amounts to 2·7% of the ash.

7. Manganese, copper, and lead are commonly, but not always, found both in the liver and spleen.

# BOOK III.

## THE ZOO-CHEMICAL PROCESSES.

# BOOK III.

## CHAPTER XVII.

### THE METAMORPHOSES OF THE TISSUES.

(306.) The reader who has carefully studied the preceding pages cannot have failed to see that four great groups of substances are essential to the well-being of the human organism.

These groups are: —

The essential factors in the animal metamorphoses.

1. The protein-bodies and their derivatives.
2. The fats.
3. The carbo-hydrates, *e.g.* sugar, starch, &c.
4. The mineral constituents of the body.

(307.) The most superficial glance at the mode in which albumen presents itself in the animal body and at the extent in which it occurs suffices to show that it must be one of the most important substances to the organism. We meet with it most abundantly in the blood and other animal juices that are most subservient to nutrition; under slightly modified forms we find it as blood-fibrin, syntonin, casein, globulin, hæmatoglobulin, &c.; and, either in its original state or in the form of some of its modifications, in the muscles, nerves, and other comparatively solid structures of the body. We further find the animal germ deposited in a fluid rich in albumen (and possibly casein), and likewise containing salts, fat, and sugar in comparatively small quantities, and there can be no doubt that it is from the albuminous matters that the germ derives the materials requisite for its nourishment.

Albumen.

We further see that the young of the mammalia are provided with a nutrient fluid — the milk — of which, besides fat and sugar, the chief constituent is casein, a protein-body rich in salts, and which, with the exception of a smaller amount of sulphur, contains the same elements as albumen, and arranged in the same proportions; at the period therefore when the growth of the gelatigenous, non-albuminous, tissues (such as the bones and skin) require the largest supplies, the body is supported by the same class of organic compounds which occur in the nutrient fluid — the blood. Hence it is obvious that the gelatigenous and elastic tissues, and in short all the nitrogenous tissues, must be primarily derived from albumen or casein: and since most of the solid tissues contain far more oxygen than the protein-bodies it is most probable that the oxygen introduced into the blood by the lungs takes an active share in converting the raw material, albumen, into the different textures; but of the individual steps of the process we know little. We are not in a position to decide with positive certainty whether blood-fibrin constitutes the necessary transition-stage from albumen to chondrin and gelatigenous tissue; nor do we know whether chondrin must always precede glutin in the formation of the connective tissue, skin, &c. It is easy to construct formulæ showing how these and other metamorphoses *may* occur; for example, by the addition of a certain number of atoms of oxygen, and the abstraction of certain atoms of water and carbonic acid, we may often construct several formulæ, all showing how the substance or tissue may be converted into other substances, and this very facility has led many good chemists to rash conclusions; and indeed when we find that the concurrence of several different substances is necessary for the accomplishment of many processes, as, for instance, that nutrient matter requires the presence of fat to be properly digested, and that not a single cell or fibre can be formed without the simultaneous presence of a protein-body (probably fibrin),

fat, and phosphates, we can hardly suppose that such formulæ as those to which we have referred can express the true and complete process of metamorphosis. That the metamorphic actions going on in the animal economy are of a complex character and require the simultaneous presence of two or more substances is a view which is further supported—(1) by the facts that wherever albuminous matters occur, non-nitrogenous carbo-hydrates are always present, although often only in small quantity, and that wherever fats are formed or decomposed, we always meet with albuminous matters; and (2) by the analogous processes which we can induce in dead organic matter, as, for instance, in the process of fermentation, where we see that one organic substance cannot co-exist with another undergoing the process of metamorphosis without being implicated in an analogous molecular movement. All, however, that we really positively know regarding the nitrogenous metamorphic products of the tissues is that the different phases under which they appear in the organism must be essentially dependent upon the inspired oxygen which gives rise to the numerous modifications which the molecules of the albuminous matters undergo before their final change into urea and similar substances.*

* In connection with the action of the inspired oxygen upon the albumen of the blood, I may allude to the interesting observations recently made by Von Gorup-Besanez (Ann. d. Ch. u. Pharm. vol. cx. pp. 86—107), on the effect produced by ozonised air on solutions of albumen and casein. Besides modifying its colour (rendering it red by incident and green by transmitted light), it produced, in an albuminous solution, fibrin-like coagula, which disappeared on prolonged action of the ozone; and there finally remained in the fluid a material which was no longer coagulable by heat nor was precipitated by mineral or organic acids, by the ordinary metallic salts (except by basic acetate of lead), or by yellow prussiate of potash, but was thrown down in flakes by alcohol, and consequently very closely resembled the albumen-peptone formed during digestion.

A solution of casein exposed for a certain time to the action of ozone became converted into an apparently albuminous fluid, being coagulable by heat, and no longer precipitable by acetic acid; and by prolonged action the further changes ensued which have been already noticed as occurring in albumen.

Ozone was found to produce no apparent action on fibrin or gelatin.

The fats.

(308.) The second great group includes the fats, whose various uses in the chemistry of the animal body have been already noticed (see p. 79). We have there shown that in addition to their mechanical uses, they take an active part in the chemistry of digestion and in all the processes by which the fluid nutrient substances are converted into tissues, and have likewise there and in other passages drawn attention to the fact that no animal cell or fibre is formed independently of the presence of fat. In connection with the importance of fat in the animal economy, we may adduce the well-known fact that the introduction of fat into the body (either as food or medicine) predisposes the organism to the formation of cells; a cell-formation of this kind however requires the concurrence of albuminous substances for the construction of the cell-walls. When the organism does not find in the food sufficient materials to form the investing membrane of the fat-cells, it borrows from the muscular fibre the necessary protein-substance; and when this source can no longer be drawn from, the fat begins to accumulate in the blood and other fluids.* From these facts and from certain microscopic observations a theory of cell-formation has been propounded, according to which each cell is primarily formed by the deposition of a thin layer of a protein-body around a minute vesicle of fat. We are not prepared fully to support this apparently simple explanation of the origin of a cell; but this at least is certain, that fat is always to be found in all highly cellular organs (as, for example, the brain and liver), and in all tissues during the process of their development; pus and certain cancerous growths are rich in fat; the hair-bulbs present an active formation of new cells, and we find them imbedded in the sebaceous glands; the chyle, which always abounds in cells in various stages of formation, always contains

* These results were deduced by Persoz and Boussingault from a series of observations on animals that were being fattened. (Ann. de Chim. et de Phys. 3rd ser. vol. xiv. p. 413—435.)

much fat; the germ in the egg is surrounded by the fatty yelk-fluid; and numerous fat-globules are found in the muscular and other fœtal tissues.

We are ignorant of the exact chemical changes which the fat in the blood undergoes; but it seems almost certain that there is a separation into base and fatty acid, and that the latter undergoes a gradual oxidation, but whether the decomposition is due to the alkali of the blood or to some other cause is not known. The fatty acid may either be thoroughly oxidised into carbonic acid and water, or may be converted into formic, acetic, and butyric acids, and in these forms be eliminated by the skin. By this oxidation the fats contribute materially to the support of the animal temperature, and have consequently been termed "heat-formers" or "respiratory food."

But the deposition of a considerable quantity of a peculiar modification of fat in the nervous tissue, shows that in this case, at all events, the fat must not be regarded as a mere material for combustion; the chemical peculiarities of the nerve-fats, their different fusion-points, and their varied distribution in different parts of the brain, tend to show that they play an important part in connection with the function of the nervous system generally, a view that is further supported by the fact that when, either from starvation or disease, the fat has disappeared from almost all the other organs, it remains unaffected in the nervous tissue.

We have already shown (see p. 27), that there is reason to believe that one fatty substance, oleic acid, contributes to the formation of the resinous acids of the bile; the individual steps of this probable metamorphosis cannot, however, be traced.

We have previously noticed the much-disputed question regarding the formation of fat within the organism, so far as the carbo-hydrates are concerned (see p. 77), but we have still to consider whether fat may not be formed from other substances, namely, the protein-bodies.

Although our attempts to convert protein-bodies into true fat by chemical means have hitherto proved unsuccessful, Liebig has shown that it is not only possible, but very probable, that these substances may be converted into fat in the animal body. In the putrefactive process, and in the gradual oxidation of albuminous substances, butyric and other fatty acids are developed; and the experiments of Quain and Virchow on the conversion of muscular tissue into adipocire, support the view that the muscular fibre is converted into ammoniacal soaps, or compounds of fatty acids with ammonia. Moreover, in fatty degeneration of muscles, the true substance of the fibrillæ disappears, and is replaced by fat.

A number of remarkable experiments have been made by R. Wagner, Donders, Middeldorpf, Michaelis, Schrader, Husson, F. W. Burdach, and others, on the introduction of various nitrogenous animal matters in the abdominal cavity, and on the metamorphoses which they undergo after being retained there for several (four to eight) weeks. Crystalline lenses, portions of coagulated albumen, and similar non-fatty protein-bodies, have been introduced into the abdominal cavities of pigeons and other birds, and after a lapse of time varying from twenty-five to fifty-four days, were found to be wholly changed, and to yield, in addition to mere traces of nitrogenous matters, a much larger proportion of fat than the substance had originally contained; and similar experiments with nearly similar results were made with tendons, cartilages, and bones. To prove, however, that the fat was formed in these cases from the introduced protein-body, and that it was not a result of infiltration from the surrounding fluid, corresponding experiments were made in which the protein-body was so enclosed (in collodion, gutta percha, glass tubes, &c.), as to cut off every possible supply of fat from without, and it was then found that when the animal juices were entirely cut off, the protein-bodies were not metamorphosed into fat, nor indeed did they undergo any essential alteration; hence, if these bodies

are actually converted into fat within the animal body, the free access of animal juices is at all events indispensable to the process. It was likewise found that porous vegetable substances, such as wood and elder-pith, when introduced like the albuminous matters, into the abdominal cavity, yielded very similar results, a yellow fatty exudation being deposited around them, and the fat having been imbibed through the intercellular spaces into the interior: and here a metamorphosis into fat was obviously out of the question.

As this method of investigation did not seem likely to decide the question of the formation of fat from the protein-bodies, Burdach has attempted another method which may, if carried more fully out, lead to satisfactory results. Some experiments which he has made on the eggs of a snail (*Linnæus stagnalis*), during their development, appear to indicate that during this process there is a considerable augmentation of fat in the embryo, which must have arisen from the decomposition of albuminous matters.* The subject, however, requires further investigation.

The carbo-hydrates.

(309.) The substances forming the third great group, the carbo-hydrates, are in many points of view so closely allied to the fats, that in speaking of them we shall have occasion to make some additional remarks regarding the uses of the latter in the animal economy. If we except cellulose, which is found in the mantles of certain tunicata (see p. 93), there are only four carbo-hydrates occurring in the animal body, namely, glycogen (or the substance forming liver-sugar), glycose or grape-sugar, lactine or milk-sugar, and inosite or muscle-sugar; and these are for the most part found in those animal fluids which are especially concerned in the nutrition and metamorphosis (the formation and disintegration) of the tissues. The fact of our finding sugar in the blood, in the

* A full account of Burdach's experiments (and indeed of almost all the investigations bearing on the subject) may be found in Hippert and Lehmann's Zoochemie, 1858, p. 544—546.

lymph, in the chyle, in both the white and yelk of egg, and in the milk, is, in itself, an evidence that this substance takes an active part in many animal processes, while a further indication of its importance is afforded by the fact of its being formed and stored up in the liver even in animals whose food contains no sugar.

Since the sugars do not, in the normal condition, pass into the excretions, but are oxidised in the blood into carbonic acid and water as ultimate products, they must, like the fats, contribute materially to the support of the animal heat; but this is by no means their only use. If they served only to generate heat, we should expect to find the saccharine matter (whether glycose or milk-sugar) diminish, or even wholly disappear in the egg during the oxidation which accompanies the process of development; but in reality an augmentation of sugar is found to take place during incubation. We shall endeavour now to indicate some of these uses. In the imperfect oxidation of the carbo-hydrates various acids (lactic, acetic, butyric, &c.) are evolved, of which one of the most important is lactic acid, which, in addition to its occurring in other parts of the organism, is found abundantly in the small intestine, as far as the middle of the ileum (see p. 186), notwithstanding the neutralising action of the pancreatic fluid and bile. It is probably of service here, in contributing to dissolve any nitrogenous matters that may have escaped the action of the gastric juice; but it is likewise an essential means of promoting the absorption of the soluble constituents of the chyle; for, from the experiments of Jolly * and of Graham † (especially the latter), it has been proved that an acidified albuminous fluid is much more diffusible than an alkaline albuminous fluid. Wherever, therefore, an alkaline and an acid albuminous fluid are separated by a membrane, the main current of the interchanging fluids will be directed

* Zeits. f. rat. Med. vol. vii. pp. 83—147.

† Phil. Trans. for 1850, p. 1.

towards the alkaline side, and hence the acid of the small intestine must essentially aid in promoting the absorption of its contents. In this way the carbo-hydrates, through their acid products of metamorphosis, play an important part in the process of chylification; and we thus probably get a clue to the therapeutic use of acids in various disorders of the chylopoietic organs.

Formation of acid phosphates.

Liebig has specially drawn the attention of physiologists to the peculiar grouping of the alkali and the acid in the animal economy, and to the necessary results of this arrangement. If the carbo-hydrates were directly consumed, without the intervention of the lactic and other acids, an acid reaction could never be generated in the bodies of herbivorous animals, or, in other words, no acid phosphates could be formed; for the ashes of plants (if we except certain seeds) always having an alkaline reaction, the food of the herbivora would (if it were not for the acids formed from the carbo-hydrates) only yield fluids with an alkaline reaction. The carbo-hydrates thus serve, by the acid products of their metamorphosis, to distribute the phosphoric acid amongst the bases; and thus to restore the acid salts and acidly reacting fluids. By this distribution of the acids and alkalies, effete matters are most rapidly removed from the tissues and transferred to the blood, where they are employed in maintaining the animal heat, or are entirely removed by the kidneys or skin, while at the same time, and by the same means, deleterious matters are hindered from passing into the tissues from the blood.

Sugar as a solvent.

Again, sugar exerts a considerable solvent action on the carbonate and phosphate of lime; and there is little doubt that the well-known augmentation of the lime-salts in the embryo of the bird during incubation is due to this action of the sugar upon the egg-shell.

Formation of fat from sugar.

We have already (see p. 77) noticed the experiments which seem to demonstrate the convertibility of the carbo-hydrates

into fat within the animal body; but we do not know in what part of the system the change is effected, nor do we understand the exact chemical nature of the change.* This much, however, is certain, that the deposition of fat within the animal body indicates a deficient supply of oxygen, and shows that the amount inspired was insufficient to allow the complete combustion of the sugar into its final products, viz. carbonic acid and water.

Further uses of sugar and of the lactic acid derived from it will be shortly noticed, in their connexion with the next great group, the inorganic salts, which we now proceed to consider.

Mineral constituents.

(310.) Any doubt that might have existed regarding the necessity of the presence of these substances for the support of animal life, must have been completely removed by the experiments which have been made by various French physiologists, showing that animals died in a comparatively short time, when fed upon substances containing no salts, although otherwise nutritious.

Antagonism of acid and alkaline fluids.

Although the latest researches of Du Bois Reymond (see p. 404) render it probable that Liebig has attached a very undue weight to the electric phenomena induced by the separation of the acid and alkaline fluids, certain results of unquestionable importance arise from this antagonism, which seem to be widely diffused through the body. Thus the blood, chyle, lymph, and transudations are always alkaline; so also are the saliva, and (less strongly) the bile and pancreatic fluid; the gastric juice is strongly acid, as also are the muscular juice after exercise (see p. 405), and the parenchy-

* Liebig has suggested two different ways in which the formation of fat from sugar may be explained. It may in the one case be analogous with various fermentations, each atom of sugar being decomposed into carbonic acid, and into a substance poor in oxygen; or in the other case the sugar may undergo a process analogous with butyric fermentation, in which the hydrogen is in part abstracted from the carbo-hydrate and carbonic acid escapes, while a substance poor in oxygen remains in the form of a fatty acid. The formation of butyric acid from sugar is explained by the formula $C_{12}H_{12}O_{12} = 4H + 4CO_2 + C_8H_7O_3.HO$.

matous fluid of the spleen, thymus gland, smooth muscles, liver, and suprarenal capsules. A similar antagonism (in a slight degree) seems to exist between the yelk and white of the egg, and probably between the blood-cells and the plasma. Now wherever a fluid exhibits an acid reaction, it is found to contain acid phosphates, and when the acid reaction is not distinctly marked, phosphoric acid is found either conjugated or simply combined with casein, hæmatoglobulin, or glycerine. The earthy phosphates are, moreover, brought into solution by free acids to a greater extent than could have been effected by albumen or casein alone (see p. 127); and in this way we can account for the large quantities of these phosphates which are present in the ash of the animal fluids; for the discoveries of Graham show that by simple physical laws, an acid fluid may be separated from the alkaline blood, or an acid phosphate may be separated from a neutral phosphate and permeate the coats of the vessels.

Phosphates.

It was first shown by Liebig, in his investigation of the muscular juice, and has been subsequently confirmed by C. Schmidt, Lehmann, and others, that those fluids which are very rich in phosphates, and which exhibit an acid reaction, contain only a small amount of soda-salts, but are very rich in potash-compounds; while the blood is rich in soda-salts and very deficient in potash-compounds. Graham's experiments show that there is a considerable difference in the diffusibility of potash and soda salts, but we have not as yet sufficient data clearly to elucidate the physical reason of this grouping of the acid phosphates and potash-compounds; nor can we tell with anything like certainty what purposes, in relation to metamorphosis generally, are accomplished by the simultaneous presence of the free acid, the phosphates, and the potash-compounds, in these animal fluids.

Potash-salts.

We likewise find phosphates in parts and tissues of the body independently of the presence of a free acid or the formation of acid salts. All histogenetic substances (see

p. 127) are so closely combined with phosphates (chiefly phosphate of lime), that they remain associated during the solution and the subsequent re-precipitation of these substances; and the ground-work of developed tissues (such as muscle, connective tissue, lung, and liver) always contains in its ash a considerable quantity of phosphates in the form of 1 equivalent of fluid to 1 of base, whence we may infer that acid phosphates existed in the recent tissue, or that a portion of the phosphoric acid had been combined with organic matter. We have already seen (p. 386) that all plastic exudations from the blood must contain a certain amount of phosphates; and C. Schmidt has shown that, in the Mollusca, a definite amount of these salts is required to supply the first basis for new tissue, even in organs which subsequently exhibit an excess of carbonate of lime.* A further and a very convincing proof of the share taken by the phosphates in the formation and functions of the tissues is afforded by the fact noticed by Liebig, that although the herbivorous animals take up a very small quantity of phosphates in their food, and although their blood is very poor in these salts, their tissues and organs contain as large a proportion of phosphates as the corresponding parts of the Carnivora.

Alkalinity of the blood.

The alkalinity of the blood is not dependent on the presence of a free alkali, but is due (see p. 107) to certain compounds of the alkalies (soda almost entirely) with albuminous substances, and with carbonic and phosphoric acids. The albumen of the blood-serum is combined with soda in two different proportions, one of these albuminates being rich and the other poor in soda; these two albuminates of soda (one of which is a neutral and the other a basic compound) are mixed together in the blood in variable proportions, and it is only in disease that free albumen is found in this fluid.

* Zur vergleich. Physiol. der wirbell. Thiere, 1845, pp. 56–60.

As a consequence of the unstable character of these combinations, the acids which are formed in or enter the blood are at once saturated, and, owing to the abundant supply of acid fluids * with which the blood is surrounded, the alkalinity of the liquor sanguinis would rapidly be destroyed if the newly formed salts were not readily and quickly decomposed into carbonates, in addition to being in part removed unchanged from the blood.

Uses of the alkalies in the blood.

We have now to consider the purposes which the alkalies accomplish in the blood. The main purpose doubtless is, the promotion of the oxidation of the constituents of the blood, oxygen being simultaneously present in that fluid. It is universally known that the tendency of oxygen to combine with certain elements is enormously increased by the presence of alkalies; and numerous experiments show the necessity that the organic constituents of the blood should be subjected to a process of gradual oxidation by the simultaneous presence of oxygen and the loosely combined alkalies in the blood. In order to obtain a clear idea of the most probable action of this process, we will notice the constituents of the blood individually, and consider their relations when exposed to the simultaneous influence of free or loosely combined alkalies and of oxygen, at the temperature of the human body.

We will begin with the organic acids which freely and in considerable quantity transude into the blood. Solutions of the salts formed by these acids with alkalies very readily undergo decomposition even if there is little air admitted, provided there be an excess of the alkali. Solutions previously colourless become brown; low fungoid growths are developed, and after a time products of the oxidation of the organic acids (usually other acids) are generated. The alkali-salts of gallic and pyrogallic acids oxidise so rapidly that they have

* According to Liebig, the lactic acid yielded by the muscular tissue alone is more than sufficient to neutralise all the alkaline fluids of the body.

been proposed by Liebig as eudiometric agents. Wöhler's discovery, that the alkali-salts of the organic acids are converted in the system into carbonates (see p. 327), is therefore nothing extraordinary, and certainly does not prove that the animal body possesses any *special* oxidising power; the means by which organic acids in combination with an alkali are consumed being precisely the same both within and without the organism.

Action of alkali on sugar.

The rapid consumption of sugar in the blood is easily accounted for, when we consider that sugar in association with an alkali can abstract oxygen from many metallic oxides, such as oxide of copper (Trommer's test), oxide of silver, &c. The combined experiments of Meyer and Bernard further elucidate the mode in which the sugar is destroyed; Meyer * having discovered that carbonic oxide is not only easily absorbed by the blood, but that it displaces an equal volume of oxygen, and thus renders it poor in this constituent; while Bernard has discovered that after the absorption of carbonic oxide by the blood, the sugar sometimes accumulates to such an extent in that fluid as to appear unchanged in the urine. The sugar is not directly oxidised into carbonic acid and water, but is first probably converted into lactic acid and some of the fatty acids; possibly the succinic acid which has been occasionally met with may also originate from sugar.

The experiments that have been made on the oxidising agency of the alkalies on the fats and fatty acids are not so striking in their results as those we have already mentioned. There can be no doubt that the alkalies in the blood, even if in the state of carbonates, are actively engaged in the saponification of the fats, but whether they co-operate with the oxygen of the blood, so as to oxidise the fatty acids that are liberated, is not positively certain.

The researches of Chevreul and Scherer show that hæmatin

* Meyer's experiments were of course made on blood that had been abstracted from the body.

when dissolved in alkalies undergoes an immediate change if oxygen be present, becoming converted into a colourless body. The exact nature of this metamorphosis is not known.

It cannot be doubted that the albuminous matters of the blood undergo a gradual oxidation before they can be employed in the formation or restoration of the tissues, but we are not able to determine the extent to which the alkalies influence their oxidation and further metamorphosis.

Oxidising action of the blood.

Lehmann has directed attention to the fact that the purely chemical character of the above change is evidenced by the definite limitation of the oxidising power of the blood. That this power, although very intense, is very limited, is demonstrated by experiments which clearly show that if more than a certain quantity of sugar or of a vegetable acid in combination with an alkali is introduced into the blood, the excess passes unchanged into the excretions. Thus the experiments of Lehmann and of Ranke show that salicin is sometimes only oxidised in the organism into salicylous acid, and on other occasions into salicylic acid, the different result apparently depending partly on difference of constitution in the persons on whom the experiments were made, and partly on the quantities that were administered. On the other hand, the action of the alkali in connection with the oxidation of the blood-constituents must not be overrated, for we find from the experiments of Parkes, Buchheim, and Clare, that the introduction of an alkali into the stomach, or even its injection into the blood, is not necessarily followed by any augmentation of sulphuric acid in the urine sufficient to demonstrate that there had been an increased oxidation of the albuminates; nor in cases of artificially induced saccharine urine does the administration or injection of alkalies or their carbonates cause a disappearance or even a necessary diminution of the sugar.* The fact noticed by G. v. Liebig, that a very active

* Although Lehmann's experiments (which are fully described in pp. 233—235 of the third volume of my translation of his "Physiological Chemistry") fully bear out the statement contained in the text, and seem to overthrow

process of oxidation goes on in the acidly reacting muscles, seems to indicate that the presence of an alkali is not an essentially necessary condition of oxidation.

Important as the oxidising process carried on in the blood doubtless is, we must recollect that many isolated facts have been noticed which are apparently opposed to the view of the process being perfectly general. Various phenomena seem to indicate the co-existence of an oxidising and a de-oxidising process; as, for instance, the formation of substances so rich in unoxidised sulphur as taurine and cystine, and of others so poor in oxygen as cholesterin, hypoxanthine, &c. Ranke's * experiments show that the animal organism exerts a positively reducing or de-oxidising power upon indigo, ordinary indigo-blue being converted, when it reappears in the urine, into sub-oxide of isatin, or reduced indigo.

Chloride of sodium.

There are strong reasons for believing that chloride of sodium is an active factor in the metamorphoses of the animal tissues. We find it in a tolerably fixed and definite quantity in most of the animal juices which are specially concerned in nutrition, the quantity in each case being wholly independent of the nature of the food or of the amount taken with the food; while the quantity in the excretions, and especially in the urine, corresponds very closely with the quantity ingested with the food. Even if we attach little weight to the instinct which leads certain domestic animals eagerly to lick up the salt placed before them, and which induces wild animals (buffaloes for instance) to travel long distances in search of salt-licks (as they are termed), or to the corresponding craving exhibited by certain African tribes for salt; the experiments of Boussingault distinctly show that the use of salt with ordinary food (unless that food

Mialhe's view that diabetes is due to a deficiency of alkali in the blood, I feel bound to state that I have on several occasions prescribed alkaline carbonates with great temporary benefit in cases of diabetes.

* Journ. f. pr. Ch. vol. lvi. p. 17.

contains a certain quantity) is indispensably requisite for the healthy condition of domesticated animals; Boussingault made simultaneous experiments upon two sets of cows (each consisting of three), one of which he fed for a month on food with which salt had been mixed, and the other on fodder containing no salt; and he found that, although the salt produced no effect upon the formation of flesh or fat, or upon the quantity of milk, there was a very marked difference in the external appearance and activity of the two sets of animals; those which had received no salt presenting a less smooth and shining coat, and being in thoroughly bad condition. The importance of this mineral constituent of the body is further shown by the fact, that in cases of starvation or of insufficient nourishment, and in certain acute diseases (especially pneumonia), the separation of common salt by the urine soon ceases, lest the blood should lose its due proportion.

The following are some of the ways in which chloride of sodium co-operates in the metamorphosis of the tissues.

Some protein-compounds, as for example albumen and casein, when they have been freed as much as possible from alkalies and salts, are soluble in a solution of chloride of sodium; whilst others, as for instance glutin and syntonin, are precipitated from their acid solutions by the addition of a solution of this salt, of less strength even than 4%. Hence the presence of chloride of sodium in such fluids as blood, exudations, &c., may serve under different circumstances to promote both the separation and the solution of albuminous substances.

Urea and grape-sugar are almost the only substances with which chloride of sodium combines chemically; and Liebig was led by this fact to very ingenious views regarding the function of salt in the metamorphosis of matter. Urea probably combines with chloride of sodium far more intimately than we should be led to infer from their ready separation

by recrystallisation in water; thus urea is only imperfectly separated by nitric acid from concentrated urine if much salt is present; and again, it occurs in association with salt even in fluids in which we should scarcely expect it, as, for instance, in the fluids of the eye and in the sweat. Hence Liebig conjectures that the absence of urea as well as of common salt in the muscular juice, and the passage of urea into the circulation, and subsequently into the urine, are due to the fact of the urea existing in the organism in a state of combination with chloride of sodium. Again, diabetic urine always contains the sugar and salt compound to which we have already alluded, in addition to free sugar; indeed it not unfrequently happens that the only saccharine crystals which we can succeed in obtaining from diabetic urine consist of this compound. Now since the saliva and pancreatic fluid, whose function it is to convert starch into sugar, and the gastric and intestinal juices, contain a considerable quantity of chloride of sodium, it seems very probable that the sugar is absorbed from the intestines in this state of combination; and this probability is much increased by the observation of Bernard, that sugar when injected into the subcutaneous cellular tissue appears more rapidly in the urine when it is mixed with chloride of sodium, than when it is injected pure or mixed with sulphate of soda.

The chloride of sodium must also undergo decomposition in the animal organism. It is impossible to decide with certainty whether the free hydrochloric acid of the gastric juice arises from the chloride of sodium, or from the more easily decomposed chloride of calcium; but at all events, in the blood of herbivorous animals it must be decomposed by the preponderating quantity of the salts of potash which is derived from their food; for in every 4 parts of alkaline carbonate in their blood-serum there are at least 3 parts of carbonate of soda, and only 1 part of carbonate of potash; while in the muscular juice both of carnivorous and herbivorous animals chloride of potassium is almost solely found. This

fact, for the knowledge of which we are indebted to Liebig, shows, on the one hand, that the chloride of sodium in the blood must necessarily undergo an interchange of constituents with the carbonate and phosphate of potash, and on the other hand, that nature has assigned very different functions in the animal organism to the alkalies which are otherwise so similar in a chemical point of view.

Liebig is of opinion that the constancy of the amount of chloride of sodium present in the blood is an essential point in connection with the process of absorption; and when we consider that the fluid contents of the intestinal canal are far less dense than the blood, and that the kidneys possess the property of immediately carrying off any excess of water that may have entered the blood, we cannot doubt that important endosmotic relations are established by the fixed concentration of the blood.

Lastly, chloride of sodium seems to exert a decided influence upon the development of cells both in secretions and exudations. Mucus, which consists almost entirely of a humid mass of cells, contains a far larger quantity of chloride of sodium than any other animal fluid; the cartilages, which are highly cellular, contain more of this constituent than any other solid tissue; the synovial fluid and the sweat also contain it abundantly. Exudations in which pus-corpuscles or cancer-cells are developed are rich in chloride of sodium; and in pneumonia the chloride of sodium which is retained in the body (and can scarcely be detected in the urine) accumulates chiefly in the pulmonary exudation, which is generally transformed into cytoid corpuscles (grey hepatisation), and partly in the saliva (Beale). We are entirely ignorant of the mode in which this salt acts in the development of cells.

With respect to the other mineral constituents which occur in the animal body, we need only refer to what has been already stated (see pp. 125—139), since they play a less active and important part in the general function of life.

# CHAPTER XVIII.

## DIGESTION.

(311.) As we have already (in the second part of this volume) treated of the different juices which take part in the digestive process, and have attempted to determine the function which each of them performs, we shall now proceed, on the assumption that the reader has an ordinary knowledge of the structural anatomy of the intestinal tract, to notice the changes which are impressed by the digestive process on the different constituents of food; namely, the mineral constituents, the carbo-hydrates, the fats, and the albuminates.

Digestion of mineral substances.

Mineral substances* usually undergo comparatively little change during the digestive process, and often enter the lacteals without undergoing any changes whatever. Carbonates and free bases are converted in the stomach into chlorides or lactates, according as hydrochloric or lactic is the preponderating acid in the gastric juice; sulphates are reduced in the intestinal canal to sulphides; the earthy phosphates are soluble in the acids of the gastric juice, and phosphate of lime is also partially soluble in carbonic acid, sugar, chloride of sodium, &c. The magnesian salts appear to undergo a certain degree of decomposition, so that a greater proportion of acid than of base is absorbed; some of the soda or potash of the intestinal fluid probably abstracting a portion of the acid from the magnesian salt. Chloride of

* In the consideration of the mineral substances I have included a few which have no right to be regarded as constituents of food, but which are of interest in relation to therapeutics.

magnesium, magnesia, and its basic carbonate ($3MgO.CO_2.HO + MgO.HO$), are all converted in the intestinal canal into the bicarbonate, most of which reappears in the excrements.* According both to Frerichs † and Bernard, metallic iron and its peroxide are soluble in the gastric juice, iron filings being converted (according to the latter observer) into protoxide and peroxide of iron in the stomachs of living animals. These salts must undergo further changes whose nature is not understood, from coming in contact with phosphates and other substances in the stomach.

The nitrates, borates, chlorates, and arseniates of the alkalies pass unchanged from the intestine into the blood.

As the salts of ammonia, after their ingestion, are found to pass unchanged into the urine, they must enter the blood unchanged.

Salts of the oxide of silver enter into combination with organic matters whenever they have an opportunity of doing so. They do this even in the mouth, and likewise in the stomach, notwithstanding the presence of hydrochloric acid; and in the latter case it is not until the albuminates (or peptones) are saturated that any chloride of silver is formed. These albuminates of silver are soluble both in acid and alkaline fluids, and it is in this form of combination that silver enters the blood.‡

The changes which the salts of mercury undergo in the organism have been carefully studied by several competent observers. Mialhe, who has paid much attention to the chemical action of remedies, maintains that calomel is converted by the alkaline chlorides of the stomach into corrosive

* See Guleke, De vi magnesiæ, etc. Dorpati, 1854; and Kerkovius, De magnesiæ ejusque salium mutationibus. Dorpati, 1855.

† The references to Frerichs in this chapter always apply to his celebrated article on digestion, in Wagner's Handwörterbuch der Physiologie.

‡ Buchheim, Lehrbuch d. Arzneimittellehre, pp. 242—244. I cannot too highly recommend this work to those who wish to study the chemical action of remedies, and the changes which they undergo in the organism.

sublimate, because if we heat calomel with strong solutions of chloride of sodium or chloride of ammonium, some of the calomel becomes converted into corrosive sublimate; but Von Oettingen and Buchheim have clearly shown that this change does not take place in dilute solutions, and that even when four times as much chloride of sodium was added to the gastric juice as is actually present, not a trace of corrosive sublimate was formed. At the temperature of the body, Von Oettingen found that calomel rapidly combined with albumen. Corrosive sublimate also enters into combination with albuminous substances, but the nature of the compound is not definitely known; most chemists regard it as an albuminate of oxide of mercury.

The changes which sulphur undergoes in the organism have been specially studied by Buchheim and Krause; but they have not come to any very decided conclusion. They find that it is not dissolved by the fatty matters present in the intestines, and are of opinion that it is probably converted into an alkaline sulphide.

Digestion of carbo-hydrates.

(312.) The carbo-hydrates next claim our attention, viz. the different kinds of sugar, starch, gum, and cellulose.

Sugar.

Of all the varieties of sugar, grape-sugar or glycose is the most important, partly from its frequent occurrence in ordinary articles of food (fruits, honey, &c.), and partly because it is the form of sugar into which other carbo-hydrates (starch, &c.) are transformed before they are fitted for absorption or for any further changes.

From the experiments of Lehmann, Uhle, and Von Becker on rabbits and other animals, it appears that when sugar is introduced in large quantity through the mouth into the stomach, it is very rapidly diffused over a large extent of the intestinal tract, and is especially abundant in the cœcum; about an hour after its ingestion the small intestine is found to contain a thin and often perfectly limpid saccharine solution, which more or less rapidly disappears from the bowels according to its degree of concentration.

The absorption of sugar from the intestine is a very slow and gradual process; and it is only rarely that we can detect absorbed sugar in the chyle or portal blood. When, however, very large quantities of sugar are introduced into the stomach, it may be detected in the blood, where it sometimes amounts to 0·6%, and any excess above this quantity is at once carried off by the kidneys.

From the fact of our finding an unusual quantity of glycose in the blood under these circumstances, there can be no doubt that a portion (probably far the largest part) is absorbed in an unchanged condition; some, however, of the sugar is always converted into acids. When sugar was injected into the stomachs of rabbits, which were killed an hour afterwards, the contents of the duodenum and jejunum were found to have a strong acid reaction, which was less marked, but still very distinct in the ileum, while the contents of the cœcum always presented a very strong acid reaction. This acid reaction depends chiefly on the formation of lactic acid from the sugar, but in the cœcum butyric acid preponderates over the lactic. From the experiments of Heintz and Van den Broek, it appears probable that the bile takes an active part in the conversion of sugar into lactic acid; others have held that the pancreatic fluid is concerned in this change. That it is not effected by either the intestinal juice or the mucus of the intestine, seems to be proved by experiments made by Funke, who introduced a solution of glycose into a tied loop of gut, and found on examination, two, three, or four hours afterwards, that most of the fluid was removed, but that the remaining portion never exhibited an acid reaction.

From the fact that sugar begins to accumulate in the blood within a short time (from one and a half to two hours) after its ingestion, we may infer that it is for the most part absorbed by the capillaries; but as we always find small quantities also in the chyle, when much sugar has been taken,

a portion of it would seem to have been taken up by the lacteals.

From numerous observations instituted by Von Becker on the absorption of sugar, the following facts seem well established: —

Laws of its absorption.

(1.) The quantity of the absorbed sugar is altogether independent of the length of the loop of gut in which it is enclosed, or of the superficial extent of the absorbing surface.

(2.) While it is generally believed that the absorption of the intestinal contents proceeds with a rapidity proportional in some degree to the dilution of the solutions contained in the intestine, Von Becker found that for saccharine solutions precisely the opposite rule held good; for it appeared that when equally large quantities of solutions of different strengths were injected, the absorption stood in a direct ratio to the concentration.

The comparative difficulty with which sugar is absorbed, as compared, for example, with various salts, is explained on purely physical grounds by the endosmotic experiments of Graham and of Jolly. It has been found, for instance, by Graham, that sugar has less than half the diffusibility of chloride of of sodium, for while 58·7 parts of salt are diffused, only 26·6 parts of sugar are diffused under precisely the same conditions.

These facts seem to explain how it is that the sugar, which is usually in a very dilute form in the intestine, is so slowly absorbed and so rapidly diffused over a large extent of intestinal surface.

It will readily be seen from the preceding observations, that in consequence of the amount of the absorbed sugar varying with the concentration, it is by no means easy to determine how much sugar an animal of given weight can absorb in a given time. If a very weak solution be introduced into the intestines it is absorbed with extreme slowness; if, on the other hand, a concentrated solution is thrown into the intes-

tine, a large quantity of water is (by endosmosis) abstracted from the blood, and the gut becomes so over-distended with watery fluid, as to interfere very materially with the respiratory actions, and often even to cause death.

Cane-sugar, according to the observations of Lehmann and Von Becker (which are however opposed to those of Frerichs), is for the most part converted before it reaches the middle of the jejunum into glycose; it was only rarely indeed that Von Becker could trace cane-sugar to this spot, even when large quantities of this substance had been introduced into the stomachs of animals (cats and rabbits). Since neither saliva, nor gastric juice, nor intestinal fluid is able to effect this change, we must conclude that it is induced by the presence of some of the other contents of the intestine, setting up a catalytic or fermenting action. That the conversion takes place in the intestinal canal, and not within the circulation, is obvious from the experiments which have been made by various observers (English, French, and German), which show that cane-sugar injected into the blood is carried away unchanged in the urine.

Sugar of milk behaves in the intestinal canal in precisely the same manner as glycose. It is very rapidly distributed over the whole of the small intestines, and can be traced, in about an hour after it has been swallowed, as far as the cœcum; it leaves an intensely acid reaction in the jejunum and ileum, which remains for three or four hours after the ingestion of the sugar.

Starch.

(313.) As an object of food, starch is by far the most important of the carbo-hydrates. We know that in consequence of its insolubility it must undergo a preliminary metamorphosis in order to be absorbed, and that it must be converted into dextrine and glycose with perhaps a little lactic acid, the saliva (see p. 151) and the pancreatic juice (see p. 181) being the chief means by which the re-arrangement of the atoms of starch is effected. Powerful as is the action

of the saliva upon boiled starch, its effect upon raw starch, especially when we consider for how short a time the starch and the saliva are being intermingled, must be very slight. The starch probably for the most part enters unchanged into the stomach, where it is generally believed that the gastric juice rather impedes than promotes any further action of the saliva upon it. The latest observations on this subject, by Drs. F. G. Smith and Brown-Sequard*, strongly tend, however, to show that the gastric juice in the stomach does not impede the conversion of starch into sugar. It is probably in the duodenum, after the pancreatic fluid has come in contact with it, that its active metamorphosis occurs; and, as we have seen in p. 185, the intestinal juice afterwards completes the metamorphosis of any starch that has escaped the effects of the saliva and pancreatic fluid.

The conversion of starch into sugar is a gradual process. The starch-granules become softened externally, and as they dissolve become converted into dextrine and sugar. Individual lamellæ peel off and become detached, and then rapidly undergo disintegration; and the farther the starch passes onwards along the small intestines so much the smaller are the granules.

The enormous development of the cœcum in herbivorous animals, and the peculiar glands which abound in the Processus vermiformis seem to indicate that the amylaceous matters are here submitted to a new metamorphic secretion, but we have no certain proofs that this is the case. As facts to a certain degree supporting the view that starch is acted upon in the cœcum, we may mention that Frerichs found butyric acid especially abundant in this part of the intestine; and that Funke found that a solution of sugar injected into the cœcum becomes rapidly converted into an acid fluid.

Dextrine, the first product of the decomposition of starch,

* Journ. de Physiologie, 1858, vol. i. p. 158.

is so rapidly converted into sugar that we only rarely find it in the intestine, and then only in small quantity.

(314.) Gum is a carbo-hydrate concerning whose uses in the organism there has been much difference of opinion. We may suppose either (1) that it is converted into sugar and then absorbed, or (2) that it is absorbed directly and without change, or (3) that it is not at all absorbed, and is consequently entirely eliminated with the solid excrements. Numerous experiments, made independently by Frerichs, Lehmann, and Blondlot, show that it is extremely improbable that even a small portion of gum is converted into sugar during digestion; if therefore gum be subservient to the purposes of life we must assume that it is absorbed in an unchanged state either by the blood-vessels or the lacteals; for there is no reason to suppose that it is likely to be converted into any substance except sugar, into which it is actually changed by prolonged digestion in dilute mineral acids. Boussingault caused a duck to swallow 50 grammes (about an ounce and a half) of gum arabic, and in the course of nine hours 46 grammes were recovered from the excrements. Lehmann daily injected 10 grammes of dissolved gum arabic into the stomach of a rabbit which was fed on cabbage leaves. Gum was found abundantly in the excrements, but not a trace could be detected in the urine; and when at the end of three days the animal was killed, four hours after its last dose of gum (10 grammes), no trace of gum could be discovered either in the chyle or in the blood. Hammond (see p. 341) found from experiments on his own person, (1) that gum is altogether incapable of assimilation, and therefore possesses no calorifacient or nutritive power whatever, but is, on the contrary, a source of irritation to the digestive organs; and (2) that in consequence of the above fact, the solids of the urine during a purely gum and water diet, are entirely derived from the waste of the tissues of the body, and the carbon exhaled by the lungs from the consumption of its fat.

Gum.

Busch, in a series of observations on a woman with an artificial anus a little below the duodenum, found that most of it passed unchanged through the fistulous opening. From a review of these experiments we must either arrive at Hammond's conclusion, that gum is altogether incapable of absorption, or else that so small a quantity passes into the animal fluids as to be incapable of detection; and in favour of this latter view it must be admitted, (1) that physical experiments prove that gum penetrates through animal membranes, although much less readily than many other substances *, and (2) that the ordinary tests for the detection of gum (silicate of potash, borax, and sulphate of iron) are not sufficiently sensitive, when applied to a mixture of organic bodies, to indicate the presence of a very small quantity of that substance.

Cellulose.

(315.) Cellulose, or the substance of the vegetable cell, is one of those substances which resist the action of all the known digestive fluids; and hence all those substances which essentially consist of cellulose re-appear unchanged in the excrements both of herbivorous and omnivorous animals; but certain chemical and anatomical facts render it not improbable that in some animals, as for instance in the beaver, and possibly in caterpillars, the cellulose may be converted into sugar.†

It is probable, from the researches of Donders and others, that the thin films of cellulose which invest young vegetable cells are dissolved in the intestines of the herbivora.

* The diffusibility of gum is only half that of glycose, and four or five times less than that of chloride of sodium; while on the other hand it is more than four times greater than that of albumen.

† As the stomach, intestines, and especially the cœcum of the beaver, are often filled to distension with fragments of wood and bark, with no detectible intermixture of soluble nutrient substances, we can hardly avoid the supposition that the digestive fluids of this animal are capable of exerting a metamorphic action upon cellulose; and in support of this view it may be mentioned, that in the beaver the salivary glands and the pancreas are enormously developed; and there is a large gastric gland peculiar to this animal, which may have something to do with the digestion of cellulose.

(316.) The route by which the fats are conducted from the food into the blood is more easily traced by the microscope than by chemical tests. Experiments on artificial digestion show that neither the saliva nor the gastric juice exerts any influence on the fats, but when fatty tissue is taken into the stomach, the connective tissue and the cell-walls are digested, and the liberated fat collects in drops of considerable size or in semi-fluid masses. In the duodenum these drops or masses disappear, and from this point downwards the fat in the intestinal canal is found to be more and more finely comminuted in proportion as the alkalinity of the intestinal contents becomes more decided.* Fats.

Although the fat is mainly absorbed by the lacteals, a portion of it passes directly into the blood, as is shown by the observations of Bruck, who detected fat-granules among the blood-corpuscles of the capillaries of the villi after the free use of fatty food; and under similar circumstances the blood of the portal vein also contains more fat than usual.

There has been much doubt and obscurity until comparatively lately as to the physical conditions under which fats which are insoluble in water, are made to penetrate the membranous walls of the intestine which are charged with watery fluids. We have already seen (p. 174) that the bile is the chief, if not the only agent in the absorption of the fats; and this view is confirmed by the fact that in animals with biliary fistulæ, by which the bile is discharged externally, extremely little fat is absorbed; and Busch similarly found, in the case already referred to, that if fat (butter or cod-liver oil) was injected through the fistulous opening into the

* Busch's observations on the woman with artificial anus seem to warrant the view that there is a causal connection between the alkalinity and the minuteness of the disintegration of the fat. For, on giving her cod-liver oil on an empty stomach, the digestive fluids which escaped through the fistula sometimes had an alkaline and sometimes (most frequently) an acid reaction; and it was noticed that the fatty particles were extremely minute whenever the reaction was alkaline.

jejunum, into which, it must be recollected, none of the contents of the duodenum made their way, most of it reappeared unabsorbed in the fæces.

Alcohol.

(317.) Although in 1838 Dr. Percy clearly proved that if alcohol were freely administered, a portion of it (or at all events of an inflammable substance closely resembling it), passed into the urine and the fluid in the cerebral ventricles, the first endeavour to trace the various changes which this fluid undergoes in the system, seems to have been made in 1847, by Bouchardat and Sandras. They found that alcohol underwent no change in the *primæ viæ*, and that it was taken up unchanged by the veins of the stomach and intestines, but not by the lacteals. In the respired air they detected small quantities of alcohol, but were of opinion that it was eliminated by the organs of excretion in an oxidised form, as water, carbonic acid, and especially as acetic acid. Their observations are confirmed by Frerichs. The discrepancy between their experiments and those of Dr. Percy may be probably due to the fact, that it is only when an excessive quantity of alcohol is introduced into the system that any traces of it can be detected in the excretions.

Duchek, in two cases out of three of dogs that were killed when in a state of intoxication, detected aldehyde ($C_4H_3O.HO$, see note to p. 19) in the blood, but could find no alcohol. The oxidation necessary to convert the alcohol into aldehyde could not have taken place in the stomach, because the oxidising action within that viscus is not stronger than in ordinary atmospheric air, and no aldehyde was found in it. Since alcohol when injected into the veins causes coagulation of the blood, but does not produce that effect when introduced into the stomach; and since, further, aldehyde when injected into the blood does not cause the blood to coagulate, but occasions intoxication; he infers, that alcohol is converted into aldehyde as it enters the absorbent vessels. After narcosis from aldehyde, acetic and oxalic acids were found in the

blood, while during the intoxication no acetic acid could be detected.

Buchheim, a higher authority on a matter of this kind, disputes the accuracy of Duchek's * view that the alcohol is converted into aldehyde, which thus becomes the actual intoxicating agent.

He observes †, that it is extremely improbable that if alcohol in its passage into the blood becomes so readily converted into aldehyde, a substance so very prone to oxidation as aldehyde should remain for a comparatively long time unchanged in the blood, instead of almost immediately undergoing further decomposition. "In fact," he observes, "Duchek has adduced no sufficient proof of the presence of aldehyde in the blood, for the odour, which other experimenters failed to detect, affords very uncertain evidence (especially when it is masked by the peculiar smell of freshly-drawn blood); and the reduction of an ammoniacal solution of silver, which Duchek observed to be produced by the blood of dogs to which alcohol had been given, is no test of the presence of aldehyde, for the distillate of a healthy dog's blood produces the same effect.‡ Further, the fact that aldehyde produces in the body the same phenomena as alcohol, is no proof of the point in question. Indeed, we possess at present no means of determining with certainty, whether it be alcohol or aldehyde that is present in the blood in these cases §; and most probably the blood contains comparatively large quantities of undecomposed spirit with traces of aldehyde." Buchheim failed in detecting the acetic and oxalic acids which had been noticed by the

* Prag. Vierteljahrsschrift, u. s. w., 1853, vol. iii. p. 104.

† Lehrbuch der Arzneimittellehre, p. 103.

‡ Masing, De Mutationibus spiritus vini in corpus ingesti. Diss. Inaug. Dorpat. 1854.

§ Strauch, De Demonstratione spiritus vini in corpus ingesti. Diss. Inaug. Dorpat. 1852. (See also Buchheim, Ueber die Nachweisung des Alkohols bei gerichtlichen Untersuchungen, in Deutsche Zeitschrift für Staatsarzneikunde, 1854.)

previous observers, but determined with certainty the presence of alcohol in the condensed respiratory products, and in the urine, both in the case of dogs and in that of two men; Massing and Strauch also detected it in the urine. Ether, he believes, undergoes the same changes in the blood as alcohol; while chloroform (which has been detected unchanged in the blood), is finally decomposed into formic and hydrochloric acids.

The protein-bodies and their allies.

(318.) We now proceed to the consideration of a group of bodies of which the protein-compounds are the main representatives, but which likewise includes not only their derivatives, chondrin and glutin, but a number of other matters, such as emulsin, the poison of serpents, curarine (or woorali), and various poisons of infectious or contagious diseases. All these bodies must not only be dissolved, but must undergo an essential change in the intestinal canal before they can be absorbed. We have already seen that the albuminous matters are not merely dissolved by the gastric juice, but are converted into matters termed peptones (see pp. 108, 163), which, although similar in their ultimate composition to the substances from which they were derived, differ from them in several essential points, amongst which may be especially mentioned their greater solubility in water, the readiness with which they pass through a filter, their being no longer coagulable, and (which is of the greatest importance in relation to digestion) their ready diffusibility through animal membranes. These peptones can be formed either by natural or artificial digestion from the gastric juice. They form a group of substances, which have the following properties in common: — They are white, amorphous, easily pulverisable when dry, are insoluble in alcohol, but dissolve readily in water, the aqueous solution having an acid reaction, and not being coagulable by heat or by acids, but being precipitable by tannic acid and by corrosive sublimate, but not by the metallic salts generally. Ferrocyanide of potassium (a most general test for this class

Peptones.

of bodies) merely induces a slight turbidity when added to a solution acidified by acetic acid; and Millon's test (see p. 104) and even chromic acid produce no apparent change. The peptones form soluble compounds with the alkalies and the alkaline earths. The different peptones, although agreeing in the above common characters, are not perfectly identical.

Meissner * has recently discovered a class of bodies which are always formed simultaneously with the peptones, by the action of the gastric juice on albuminates. These bodies, to which he has assigned the name of parapeptones, are distinguished from the peptones in being precipitated from the acid digestive mixture in the stomach by the addition of a little alkali. (The alkali must not be added in sufficient quantity to neutralise the acid fluid.) These parapeptones, though differing slightly from one another, have the following properties in common. They are insoluble in water, but form easily soluble compounds with acids, alkalies, and alkaline earths. Alcohol has no effect upon the solutions of these compounds, but a mixture of alcohol and ether throws down white flakes. Millon's test gives the same reactions with the parapeptones as with the albuminates; while they contrast with the peptones in this respect, they coincide in forming pure blue solutions with sulphate of copper and potash, while the unchanged protein-bodies form with these substances bluish violet solutions. From these and other reactions which Meissner has described we should infer that the parapeptones are more nearly related than the peptones to the protein-bodies from which each derives its origin; and we might hence be inclined to infer that the peptones are formed from the parapeptones, and that the latter are merely imperfect products of gastric digestion. Meissner however shows very clearly that this is not the case, and that the albuminates are

Parapeptones.

* Zeitsch. f. rat. Med. 1859. 3rd Ser. vol. vii. pp. 1—16.

apparently simultaneously decomposed (or broken up) into peptones and parapeptones, which latter are not further changed by the gastric juice. From several experiments he concludes that the protein-bodies are broken up into peptones and parapeptones, which stand to one another in nearly the ratio of 2 : 1. Although the gastric juice cannot affect parapeptones, they are converted into peptones (or very similar bodies) by the action of pancreatic juice.

We are indebted to Mulder for the knowledge (and he has been confirmed by Meissner) that gelatin and the gelatigenous tissues do not yield peptones. Meissner found that a solution of pure gelatin in gastric juice contained neither peptone nor parapeptone, but gelatinised on cooling, and behaved precisely as it would have done if dissolved in dilute hydrochloric acid, being in fact altogether unchanged. Busch, however, obtained very different results. On giving gelatin (calves' foot jelly) to his patient, the fluid discharged from the fistulous opening contained only one-third of the gelatin that had been administered, and this portion had lost its property of coagulation.

**Emulsin.** (319.) Emulsin seems to be thoroughly metamorphosed in the intestinal canal, for if this substance and amygdalin are simultaneously introduced into the stomach or into the blood, decomposition is set up in the amygdalin (which taken alone is harmless) and prussic acid is formed, which destroys the life of the animal on which the experiment is performed. Lehmann allowed rabbits to eat sweet almonds (which contain emulsin), and injected amygdalin into the jugular vein one, two, four, and six hours after they had fed, and the animals remained perfectly well. He then reversed the experiment and injected emulsin into the vein while he introduced a solution of amygdalin into the stomach of the animal, and in this case symptoms of poisoning by prussic acid very soon presented themselves. The only way of accounting for these results is by supposing either that the emulsin is so completely

changed in the *primæ viæ* that it can no longer set up decomposition in the amygdalin, or that the emulsin is incapable of being absorbed. If the latter were the case it would pass off unchanged by the excrements, but Lehmann found that on mixing amygdalin with the excrements of a rabbit which had been fed for forty-eight hours on sweet almonds there was no trace of any solution of prussic acid. Indeed no decomposition of the amygdalin was induced even by the contents of this animal's cœcum. Kölliker and H. Müller have repeated and confirmed Lehmann's experiments.

Curarine (or woorali) and the other poisons which we have mentioned seem to be changed in a similar manner in the intestinal canal, for otherwise they would be as poisonous when taken into the stomach as they are when introduced directly into the blood. Curarine.

(320.) The gastric juice is the chief but not the only agent that exerts a metamorphic effect on the protein-bodies. The quantity of gastric juice which is secreted is usually not sufficient to dissolve and metamorphose the amount of albuminous matters which is necessary for the due nutrition of the body; hence a considerable portion of this class of bodies passes unchanged from the stomach into the small intestines, where it is acted upon by the intestinal fluid and probably also by the pancreatic juice.* Any protein-bodies The various intestinal solvent fluids.

* The true action of the pancreatic juice on the albuminates is not definitely determined. While Frerichs, and Bidder and Schmidt deny that the pancreatic juice has any action on these bodies, Corvisart in 1857 published a memoir "On the Digestion of Nitrogenous Alimentary Bodies by the Pancreas," which has led to much discussion. In this memoir he relates a number of experiments upon animals, the results of which led him to the conclusion that the pancreatic juice, whether alkaline, neutral, or acid, possessed a true digestive action, and converted the protein-bodies into peptones. Keferstein and Hallwachs (Göttingen Nachrichten, 1858, No. 14), directly deny the correctness of his conclusions. Meissner (op. cit.) finds that the pancreatic juice is able to digest albuminous substances, and that it transforms them into bodies closely allied to the peptones, provided the fluid that is used (namely, the infusion of the pancreas) be prepared from animals which were killed while in the act of digestion, and provided also that the fluid has an acid reaction. The former of

that may make their way into the large intestine most probably escape without further change in the excrement.

The casein of milk is precipitated in the stomach in the form of flakes and is then gradually dissolved, but if a considerable quantity of milk was given to Busch's patient a portion of the casein passed, without being coagulated, out of the fistulous opening. Soluble albumen on the other hand appears, from experiments on artificial digestion, not to be coagulated, but to be converted directly into peptones and parapeptones. Busch found that on giving his patient uncooked white of egg a portion was absorbed in the stomach and the part of small intestine above the fistula while a portion (about one-third) escaped unchanged.

Busch made numerous observations on the action of the intestinal juice on coagulated albumen, flesh, starch, &c., but as they for the most part coincide with those of Frerichs, and Bidder and Schmidt it is unnecessary to notice them.

Absorption of the peptones.

(321.) The protein-bodies after their conversion into peptones are for the most part absorbed by the lacteals; a

these conditions accords with Corvisart's own observation, the latter is opposed to it. In his latest publication (L'Union Méd. 1859, No. 87), while noticing the criticisms to which his views have been exposed, he gives the following as his conclusions. (1.) That the mixed liquid poured into the duodenum (namely the bile and the pancreatic and intestinal juices) digests albumen when the gastric juice is altogether excluded. (2.) That coagulated albumen can be digested in large quantity by the infusion of pancreas alone; and (3.) That the quantity of albumen which is dissolved is almost the same (notwithstanding Meissner's assertion) whether the fluid is acid, neutral, or alkaline, and that in point of fact the mixture of fluids in the duodenum is sometimes acid, sometimes neutral, and sometimes alkaline, and that, notwithstanding their difference of reaction, the effect on albumen is much the same. Corvisart further holds that the pancreas is not in full action till about five or six hours after a meal; in short, not till the stomach has almost completed its work. Experiments by Dr. Brinton and Professor Harley in part confirm Corvisart's views. The latest investigations are those of Skrebitzki (conducted under the superintendence of Bidder and Schmidt), who comes to the conclusion, from a series of careful experiments, that the solvent action of the pancreatic juice is precisely equal to the solvent power of an equal quantity of water containing as much alkali as is usually found in this secretion.

portion of them is however taken up directly by the capillaries of the villi; and some authorities of great weight, amongst whom we may mention Frerichs and Donders, believe that most probably the absorption of the peptones commences in the stomach.

Daily amount of intestinal fluids.

(322.) In several points of view a knowledge of the daily amount of the secreted digestive fluids is important. The results of the investigations of Bidder and Schmidt on the lower animals show that the amount of the juice which flows into the intestinal canal in the twenty-four hours is far greater than is commonly supposed, and amounts to almost the sixth part of the whole weight of the body, and subsequent observations on the case of Catherine Kutt (see p. 162) show that probably their estimate of the amount of the gastric juice is too low.

If we apply to the case of an adult man the quantitative relations of the individual secretions obtained by Bidder and Schmidt for animals, it follows from their calculations that an adult man weighing 64 kilogrammes (or about 10 stone), will secrete in the twenty-four hours,—

| | Kil. | Lbs. | | Grammes. | Drachms. | |
|---|---|---|---|---|---|---|
| Saliva amounting to | 1·6 | (= 3·5) | containing | 15 | (= 3·8) | of solid matter. |
| Bile „ | 1·6 | (= 3·5) | „ | 80 | (=20·5) | „ |
| Gastric juice | 6·4 | (= 14·1) | „ | 192 | (=49·3) | „ |
| Panereatic juice | 0·2 | (= 0·44) | „ | 20 | (= 5·1) | „ |
| Intestinal juice | 0·2 | (= 0·44) | „ | 3 | (0=0·76) | „ |

According to these numbers, the quantity of fluid which is effused daily into the intestinal canal amounts to 10 kilogrammes, or more than 22 lbs., and is larger than the whole amount of the blood contained in the body; as farther, it only contains 310 grammes (or 3·1%) of solid constituents, it seems especially designed to rinse and purify the dissolved food.

Busch's observations on a woman with fistula in the jejunum.

(323.) Busch found, in the series of experiments to which we have so frequently referred, that the nature of the food had a very marked effect upon the amount of the secreted digestive fluids. Animal food caused a much more copious

flow of digestive fluids through the fistulous opening than vegetable food; and the most abundant effusion was noticed to follow the ingestion of fat. Busch found that, at the lowest estimate yielded by his observations, the amount of digestive fluids effused into the upper part of the intestinal canal in twenty-four hours is one-seventeenth of the weight of the body.

The experiments that have been made with a view to determine the amount of nutriment that can be absorbed by the intestinal canal in a given time, are not of a very satisfactory character. Lehmann is of opinion that a man can absorb in one hour about 430 grammes (or about 22 ounces) of sugar, 45 grammes (or about an ounce and a half) of fat, and 100 grammes (or rather more than 3 ounces) of protein-substances.

A chapter on "The Digestion," would obviously be imperfect if it included no notice of the digestibility of the different ordinary articles of food. Unfortunately, our knowledge on this subject is very imperfect, the experiments which have been made being in part unsatisfactory in the mode in which they were devised, and in part, giving absolutely contradictory results. The experiments of Gosse, who possessed the power of vomiting at will, and who thus brought up food which had remained for different lengths of time in the stomach, and even the much more valuable observations of Beaumont on Alexis St. Martin, are unsatisfactory in the following respects. (1.) These observers regarded the digestive process as ended when the food in the stomach had been reduced to a uniform pulp, and altogether neglected the changes impressed upon the food beyond the stomach. (2.) They used mixed, variously prepared, often half vegetable and half animal food, a method which is totally unfit for determining the digestibility of individual articles of diet. (3.) No mention is made, at least in Beaumont's experiments, of the quantity of food that was taken, or of how minutely it was divided. Without

entering into details of the discrepant observations made on this subject by Schultz (who at a certain time, after feeding dogs and cats with different kinds of food, killed them and examined the contents of their stomachs), and by several other physiologists, it is sufficient to quote the opinion of Blondlot, who first introduced into physiology the operation of artificial gastric fistula, and who obtained such very indefinite and inconclusive results, that he was led to express the view that the digestibility of different articles of diet depended solely on the state of the stomach at the time of the experiment, and that it is pure waste of time to labour at the determination of the digestibility of individual articles of food.* Busch found in his case of intestinal fistula that flesh, eggs, and vegetables, began to appear at the fistulous opening in from fifteen to thirty minutes after they were swallowed, but that if a copious meal had been taken, traces of these substances continued to appear for three or four hours. He gives the following results: —

| | | |
|---|---|---|
| Boiled eggs | appeared | in 3 expmts. after 26, 20, and 35 min. |
| Cabbage | „ | in 2 expmts. after 19 and 15 min. |
| Flesh | „ | in 2 expmts. after 30 and 22 min. |
| Parsneps | „ | after 12 minutes. |
| Potatoes | „ | after 15 minutes. |

The following table, extracted from Busch's memoir, is deserving of attentive study, as showing how much of each of the articles of food mentioned in the first column was absorbed before reaching the fistula in the jejunum.

* The reader who may wish for further information on this subject is referred pp. 312—321 of the third volume of Lehmann's "Physiological Chemistry," where he will find an account of the principal experiments made by himself and other observers on the digestibility of soluble and coagulated albumen, of coagulated blood-fibrin, of muscle and of pure syntonin, of casein, of the fats, and of starch.

| | Ratio of weight of food to weight of matters subsequently discharged through the fistula. | Ratio of solid constituents of food to solid constituents of the matters discharged through the fistula. | Ratio of solid constituents of undissolved portion of discharged matters to the solid constituents of the dissolved matters. |
|---|---|---|---|
| Gelatin | 1 : 3·675 | 1 : 0·94 | |
| Boiled eggs | 1 : 2·73 | 1 : 0·76 | 1 : 2·3 |
| Flesh | 1 : 1·73 | 1 : 0·35 | 1 : 2·27 |
| Milk | 1 : 1·25 | 1 : 0.62 | 1 : 4·3 |
| Parsneps | 1 : 1·2 | 1 : 0·49 | 1 : 0·94 |
| Cabbage | 1 : 0·91 | 1 : 0·58 | 1 : 0·66 |
| Potato soup | 1 : 0·7 | 1 : 0·53 | 1 : 1·5 |

From the experiments on which these numerical results are based, Busch concludes that flesh is more digestible than eggs, that parsneps are more digestible than potatoes or cabbage, and potatoes more digestible than cabbage.

## CHAPTER XIX.

## RESPIRATION.

(324.) The process of respiration consists essentially in an interchange of certain gases between the blood or nutrient fluid, and the external air,—an evolution of carbonic acid and an absorption of oxygen, which takes place, except in the lowest animals, in definite organs, known as lungs, gills or branchiæ, and tracheæ. Very low in the animal scale, as in intestinal worms, numerous zoophytes, infusoria, &c., we have no definite respiratory organs, the necessary interchange of gases taking place through the external surface of the body generally. Nature of the process.

Passing over the description of the different modes of carrying on experiments on respiration (for an account of which we may refer to Lehmann's Physiological Chemistry, vol. iii. pp. 330—332, or to any of our larger works on Physiology), we proceed at once to the consideration of the general results which have been yielded by the most important investigations regarding the interchange of gases in the lungs.

The blood in the lungs gives off carbonic acid and aqueous vapour to the inspired air, and takes up oxygen from the latter; a very small quantity of nitrogen also commonly passes from the blood into the respired air, although under certain conditions the opposite sometimes occurs.

(325.) The first point in the chemistry of the respiration is to determine the ratio between the inspired oxygen and the exhaled carbonic acid. It is well known, that the volume of carbonic acid is equal to the volume of the oxygen which is Ratio of inspired oxygen to exhaled carbonic acid.

contained in it. If, therefore, a volume of carbonic acid were found in the expired air which was equal to that of the oxygen which had disappeared from the inspired air, we might be led to infer that the oxygen which is absorbed in the pulmonary vesicles, is exactly sufficient to form the carbonic acid which they exhaled. This however is not usually the case, for under ordinary relations, the volume of oxygen which is absorbed is much larger than the volume of carbonic acid which is exhaled, the oxygen serving not merely for the oxidation of the carbon, but also for that of the hydrogen of the animal constituents. If, for instance, animals be confined in a closed vessel, we find on analysing the air which has been modified by their respiration that more free oxygen has disappeared than could have been employed in the formation of the carbonic acid that has been simultaneously evolved. On an average, for every volume of absorbed oxygen, there is only about 0·8516 of a volume of carbonic acid in the expired air; so that about one-seventh of the inspired oxygen has to be otherwise accounted for.

Volume of expired air.

(326.) The volume of the expired is always greater than that of the inspired air, partly because its temperature is higher (from 97·2 to 99·5°, according to Valentin), and partly because it is usually much more saturated with aqueous vapour than the inspired air. If however we examine both kinds of air when freed from water and reduced to the same temperature, we find a diminution of the volume of expired air corresponding to the volume of oxygen which has been absorbed, and has not been converted into carbonic acid. The small quantities of nitrogen which are absorbed or exhaled are (as we shall immediately show), too trifling to modify the result, and may be neglected.

Amount of exhaled aqueous vapour.

The quantity of water, in the form of aqueous vapour, that is exhaled by an adult man in 24 hours, has been variously estimated by different observers. Valentin calculates it at 506 grammes, or about 14 ounces, and Vierordt at 360 grammes, or about 11 ounces.

Variations in inhaled and exhaled nitrogen.

The quantity of nitrogen in the air does not remain precisely the same during respiration, but the difference is so slight that it was for a long time a disputed point, whether an excess of nitrogen was absorbed or exhaled during respiration. Recent investigations show that there is an excretion of nitrogen, although only in extremely small quantity; the relative weights of the excess of exhaled nitrogen over the quantity in the inhaled air, and of the expired carbonic acid being nearly as 1 : 100. A portion of this nitrogen occurs in the expired air under the form of ammonia. When the same air has been so repeatedly breathed by animals enclosed in a bell-jar or other vessel, that asphyxia is imminent, the ratio of the nitrogen to the carbonic acid is found to be much increased.*

Volatile matters in expired air.

In addition to slight traces of ammonia, the expired air frequently contains volatile substances that have been taken with the food, such as alcohol, phosphorus, camphor, ethereal oils, &c.; and even when no such substances can be detected in the food, the fact that the sulphuric acid, which is used for drying the expired air, always becomes reddened, indicates that traces of some organic carbo-hydrogen must be present. The experiments of Regnault and Reiset seem to establish the fact that appreciable quantities, both of hydrogen and protocarburetted hydrogen, are exhaled from the lungs when in a perfectly normal condition.

* Although the researches of Regnault and Reiset establish the result given in the text for mammals and birds, it is not universally true. The same observers found that there was little or no excess of nitrogen in the air expired by batrachians (frogs and tritons), while in fishes there is an actual absorption of nitrogen to a very considerable extent. Various conditions have been found to modify the amount of the exhaled nitrogen. Regnault and Reiset ascertained that a fowl which in summer exhaled 12 parts of nitrogen to 1000 of oxygen which it consumed, in winter exhaled only 2 parts of nitrogen to the same quantity of absorbed oxygen; and that during hybernation nitrogen was absorbed. The same observers found that during an entire deprivation of food, nitrogen was often absorbed by the lungs, and that the same was the case with animals whose health had been affected by improper food.

Percentage of carbonic acid in exaled air.

(327.) The air expired by a healthy man in a state of repose, contains on an average 4·334 per cent. by volume of carbonic acid. According to Scharling a muscular adult man exhales in twenty-four hours 867 grammes, or 27·8 ounces of carbonic acid (or about 27·058 cubic inches, reckoning the barometer at 29·9 inches, and the temperature at 32°); while according to Boussingault about 8 grammes (or rather more than half an ounce) of nitrogen, and according to Valentin about 500 grammes (or about 16 ounces) of watery vapour are also exhaled in the same period. As about 746 grammes, or about 23·3 ounces of oxygen are inhaled during that period, it has been shown by calculation that about 116 grammes, or rather more than three ounces, of that gas are retained in the organism.*

Influence of rapidity of respiration on amount of carbonic acid.

(328.) It has been proved by Vierordt that the amount of carbonic acid in the expired air is very dependent on the frequency of the respiratory movements. Having ascertained, by numerous careful observations on himself, that the carbonic acid in 100 volumes of his expired air, when breathing normally nearly twelve times in a minute, amounted to 4·334 volumes, he tried the experiment of doubling the rapidity without diminishing the normal depth of the inspiration; and he found that the relative quantity of carbonic acid was about ·907% less than in normal undisturbed respiration; when the number of inspirations was increased to three times their former amount, this diminution amounted to 1·125%; when the number was increased four-fold, the diminution amounted to 1·292%; and finally, when they were increased eight-fold, the diminution amounted to 1·600%. When the number of inspirations was diminished by one half (when six instead of twelve inspirations were taken in the minute), there was an excess of carbonic acid to the amount of 1·316%.

* These numbers are given by Lehmann in his Lehrbuch, Handbuch, and Zoochemie, but I do not clearly understand how he has arrived at this result.

These results stand out more clearly in the following tabular arrangement: —

| Acts of respiration in one minute. | Carbonic acid in 100 volumes of expired air. |
|---|---|
| 6 | 5·528 |
| 12 | 4·262 |
| 24 | 3·355 |
| 48 | 2·984 |
| 96 | 2·662 |

From these and other observations of a similar character, Vierordt has been able to show (after introducing certain corrections) that the number of respirations is a function of the number expressing the corresponding percentage of carbonic acid. Thus, for every expiration without reference to its duration, there is a constant amount of carbonic acid (of $2{\cdot}5\frac{0}{0}$), to which we must add a second and variable amount which is proportional to the duration of the expiration. The following table will elucidate our meaning: —

| Respirations. | Total percentage of $CO_2$. | Constant percentage. | Varying percentage. |
|---|---|---|---|
| 6 | 5·7 | 2·5 | 3·2 |
| 12 | 4·1 | 2·5 | 1·6 |
| 24 | 3·3 | 2·5 | 0·8 |
| 48 | 2·9 | 2·5 | 0·4 |
| 96 | 2·7 | 2·5 | 0·2 |

Now, if the respirations are 6 in the minute, each respiratory act has a duration of 10″; if they are 12 in the minute, each has a duration of $\frac{1}{2}$ of 10″, and so on; hence, taking 10″, 2·5, and 3·2 as constants, we have this relation connecting the duration of the respiration with the amount of carbonic acid: —

A respiration lasting —

| | | |
|---|---|---|
| 10″ | yields air containing | $2{\cdot}5+3{\cdot}2$ of carbonic acid. |
| $\frac{1}{2}$ of 10″ | ,, | $2{\cdot}5+\frac{1}{2}$ of 3·2 ,, |
| $\frac{1}{4}$ of 10″ | ,, | $2{\cdot}5+\frac{1}{4}$ of 3·2 ,, |
| $\frac{1}{8}$ of 10″ | ,, | $2{\cdot}5+\frac{1}{8}$ of 3·2 ,, |

and so on, till we come to the limit beyond which we cannot count the respiratory acts.

According to Vierordt's experiments about 30·5 cubic inches of air are expelled by one expiration while the breathing is undisturbed. If we assume that during hurried respiration an equally large quantity of air is expelled by expiration (which however is hardly likely to be the case), we may easily calculate the absolute amount of carbonic acid exhaled in a minute. The results are as follows:

| Number of respirations in one minute. | Carbonic acid in 100 volumes of expired air. | Cubic inches of air expired in one minute. | Cubic inches of carbonic acid expired in one minute. | Cubic inches of carbonic acid exhaled in one expiration. |
|---|---|---|---|---|
| 6 | 5·7 | 185 | 10·5 | 1·7 |
| 12 | 4·1 | 375 | 13·4 | 1·3 |
| 24 | 3·3 | 750 | 24·4 | 1·0 |
| 48 | 2·9 | 1500 | 42·5 | 0·88 |
| 96 | 2·7 | 3000 | 80·0 | 0·82 |

Although several other causes exert a decided influence on the quantity of carbonic acid in the exhaled air, there can be no doubt that this law holds good for otherwise similar conditions, and we must agree with him in holding it proved that "the rhythm of the respiration acts as the most powerful regulator of the excretion of carbonic acid."

The depth or intensity of the individual respirations exerts a similar influence on the excretion of carbonic acid. The following decisive results have been obtained by Vierordt.

| | Per cent. of carbonic acid. |
|---|---|
| If the air in a normal respiration contains | 4·60 |
| The air in a respiration twice as deep contains* | 4·00 |
| " " three times " | 3·70 |
| " " four times " | 3·38 |
| " " eight times " | 2·78 |
| " " half " | 5·38 |

* The slight apparent discrepancy between the results in this and the preceding table, is due to certain corrections having been introduced by Vierordt in the present one.

(329.) The quantity of carbonic acid in the air in the upper and lower portions of the lungs differs very considerably. According to Allen and Pepys, whose observations were made more than half a century ago, the first portion of the air yielded by a deep expiration contained from 3·5 to 5% of carbonic acid while the last portion yielded as much as 9·5%. To investigate this point, Vierordt made seven experiments, in which he divided each expiration as nearly as possible into two equal parts, and found that the carbonic acid contained in the air breathed during the first half of the expiration amounted to 3·72%, while that contained in the second half amounted to 5·44%. This result shows that Allen and Pepys had greatly overestimated the difference in the percentage of carbonic acid, and accords closely with the result of Jurine, who, in dividing expirations into four equal portions, found the values of carbonic acid in the first and last to be in the ratio of 1·01 : 1·51. He likewise obtained a similar result by comparing the amount of carbonic acid in a normal expiration with that in the air obtained by an intensely forced expiration. As a mean of eight experiments he found that while the carbonic acid of a normal expiration of 34 cubic inches amounted to 4·63%, a most complete and full expiration of 111 cubic inches contained 5·18%. The carbonic acid in the two cases amounted to 1·64 and 5·82 cubic inches; hence in the deeper portion, amounting to 77 cubic inches, there are 4·12 cubic inches, or 5·43% of carbonic acid, and therefore 0·80% more than are contained in the air given off in a normal expiration. Vierordt calculates that the air in the pulmonary vesicles contains as much as 5·83% of carbonic acid and therefore 1·2% more than is contained in a normal expiration.

Excess of carbonic acid in last part of an expiration.

(330.) It has been shown by the independent observations of Vierordt and Horn that if the respiration be suspended for a given time (varying in these experiments from 10 to 100 seconds) the expired air contains a considerably less total

Influence of partial suspension of respiration.

quantity of carbonic acid than it ought to do, but a considerable relative augmentation of that gas. This relative augmentation is clearly shown in the following results obtained by Becher.*

| | | Seconds. | | |
|---|---|---|---|---|
| Respiration stopped for | | 10 | . 3·636% | of carbonic acid. |
| ,, | ,, | 20 | . 5·552% | ,, |
| ,, | ,, | 40 | . 6·265% | ,, |
| ,, | ,, | 60 | . 7·176% | ,, |
| ,, | ,, | 80 | . 7·282% | ,, |
| ,, | ,, | 100 | . 7·497% | ,, |

Influence of artificial atmospheres.

(331.) We proceed to the consideration of the changes induced by the inhalation of artificial atmospheres, or different kinds of gas. The experiments of Regnault and Reiset on dogs and rabbits, show that the respiration of air which is richer in oxygen than the atmosphere, does not produce any marked results; the animals did not exhibit any distress from the inhalation of air containing two or three times more oxygen than our atmosphere, and the products of respiration were in no way affected.† W. Müller has attempted to determine the extent to which the oxygen may be diminished in an atmosphere without affecting the action of respiration. He finds that an atmosphere containing 14·8% of oxygen (or about two-thirds of the quantity contained in common air), exerts no apparent deleterious action on the respiratory pro-

Of excess of oxygen.

* Zeitsch. f. rat. Med. New Ser. vol. vi. pp. 249—287.

† Lavoisier and Séguin, and Allen and Pepys (from observations on man), and Marchand (from observations on the frog), came to the conclusion that although the excretion of carbonic acid was not (to any appreciable extent) increased by the respiration of pure oxygen, far more (Marchand says twice as much) oxygen is retained in the blood than in ordinary respiration. Bernard has observed that animals in an atmosphere of pure oxygen exhibit great excitement and activity. Their lips are of a bright red tint, and their blood presents an arterial character, the circulation is rapid, the secretions increased, and the muscles contract with energy. The urine of rabbits during the process of digestion is alkaline, but if they are placed in an atmosphere of oxygen, the urinary secretion becomes acid in a quarter of an hour, and is found to contain an excess of urea.

cess; but that if the oxygen is reduced to 7% (or one-third of the ordinary quantity), the animals are observed to take deeper and more forcible inspirations; while if it is reduced to 3% they rapidly die with symptoms of suffocation.

Of excess of carbonic acid.

Pure carbonic acid cannot be inhaled, because the glottis spasmodically obstructs its passage. Marchand found in experiments on frogs, that when they were made to inhale an atmosphere rich in carbonic acid (but not so rich as to be irrespirable) less oxygen was absorbed; and less carbonic acid, but more nitrogen was exhaled than in ordinary respiration. Bernard found that animals can live in air till (by their repeated respirations) its carbonic acid has increased to 12 or even 18%; if however, they are at once transferred from the pure air to an atmosphere containing such a per-centage of carbonic acid, they are immediately killed, even though an abundance of oxygen be simultaneously present. W. Müller found that animals placed in closed vessels of sufficient size, are not affected by the gradual augmentation of the carbonic acid, until they have absorbed about a third part of their bodily volume of carbonic acid. Symptoms of narcosis, such as coldness of the extremities, slowness of the respiratory acts, and rapidity (combined with weakness) of the heart's action, then set in; and after the animal has absorbed 56 or 58% of its own volume of carbonic acid, death ensues without any convulsive actions, although plenty of oxygen for the support of life still remains.

Of excess of nitrogen.

It appears from Legallois' experiments on guinea pigs, that in an air which is richer in nitrogen than the atmosphere, nitrogen is absorbed, and less than the normal quantity of carbonic acid exhaled; there appears also to be an increased absorption of oxygen.

The inhalation of pure nitrogen is speedily followed by symptoms of suffocation, but during the short time the experiment can be continued, rather an excess of carbonic acid is exhaled.

Respiration of nitrous oxide.

The respiration of nitrous oxide induces pleasurable sensations, considerable excitement, and a state resembling intoxication, which after the lapse of five or ten minutes passes into asphyxia. According to Sir Humphry Davy, carbonic acid is given off in no larger quantity than usual, but Zimmermann found that a rabbit, which in atmospheric air exhaled 0·8 of a gramme of carbonic acid in one hour, exhaled 1·3 grammes in nitrous oxide gas.

Of hydrogen.

Respiration may go on for a considerable time in an atmosphere containing hydrogen gas, if a sufficient quantity of oxygen be present. Regnault and Reiset placed rabbits and dogs in atmospheres in which almost all the nitrogen had been replaced by hydrogen (from 55 to 77% of hydrogen, from 1·1 to 14·4% of nitrogen, and from 21·8 to 28·8% of oxygen), and the rabbits inhaled this mixture for 20, and the dogs for 10 hours, without any apparent injury, except that the respiration was increased in force. At the close of the experiment, nearly the original quantity of hydrogen was found, but rather more than the usual quantity of oxygen had been absorbed. It is clear from these experiments, that the only reason why respiration cannot be carried on for any length of time in pure hydrogen gas is, that the organism is thus deprived of the oxygen necessary for life. Marchand found that frogs died in from half an hour to an hour after being placed in pure hydrogen gas, but that during this time they developed more than three times as much carbonic acid as they would have done in the same period in atmospheric air.

Of carbonic oxide.

Carbonic oxide, when mixed even in very minute quantity (0·54% according to Leblanc*, or 0·6% according to Bernard) gives rise to faintness, feelings of suffocation, stupefaction, and death. Leblanc has shown that it is to this constituent that choke-damp owes its fatal effects. The mode in which it

* Compt. Rend. vol. xxx. p. 483.

proves fatal is illustrated by the observations of Meyer, who finds that it combines very readily with the blood and displaces the oxygen.

(332.) We now proceed to notice the effects produced by various atmospheric conditions upon the respiration and its products. Atmospheric influences.

The temperature of the atmosphere first claims our attention. As Spallanzani, and several subsequent observers had noticed that hybernating animals (marmots, bats, and hedgehogs) exhaled least carbonic acid at a low temperature, when their vital activity was more or less depressed, it was assumed as a general proposition that a depression of the surrounding temperature would constantly produce this effect in all classes of animals. Letellier, however, shows in his experiments upon several different kinds of birds and mammals that the largest relative amount of carbonic acid is exhaled at a temperature between 23° and 37°, and the smallest between 82° and 109°. The difference was more marked in birds than in mammals. None of the animals could bear a higher temperature than 109° or 110°. Marchand has obtained many similar results with frogs, except that they fell into a torpid state at between 35° and 37°, when they excreted a remarkably small amount of carbonic acid. The action of the increased temperature is probably of an indirect nature, the result being apparently due to a diminution both of the number and of the depth of the respiratory acts. Vierordt has ascertained that at high temperatures less than the usual quantity of aqueous vapour is given off.

Vierordt has calculated a table of the respiratory functions from 37° to 75°. We have divided the total result into two parts, one representing the means of the values obtained at the lower degrees of temperature from 37° to 56°, and the other those between 57° and 75°.

| | Average Temperature. 47·2° | 67° | Difference. |
|---|---|---|---|
| Pulsations in one minute | 72·93 | 71·29 | 1·64 |
| Respirations „ | 12·16 | 11·57 | 0·59 |
| Volume of one expiration | 33·5 cubic in. | 31·8 cubic in. | 1·7 cubic in. |
| Air expired in one minute | 407·0 „ | 367·2 „ | 39·8 „ |
| Carbonic acid „ | 18·3 „ | 15 7 „ | 2·6 „ |
| Carbonic acid in 100 parts of expired air . . . | 4·48 | 4·28 | 0·2 |

Dr. E. Smith *, in his memoir "On the Chemical and other Phenomena of Respiration," has fully investigated the effects of the different seasons on the respiratory process, and to some extent overthrown the above conclusions. "There are," he observes, "great variations from season to season, so that as the hot season advances, all the respiratory phenomena are lessened. The diminution in myself at the middle of August was 30 per cent. of air, 32 per cent. in rate of respiration, and 17 per cent. of carbonic acid. In Mr. Moul (one of the gentlemen experimented on) to the middle of June, the diminution was 27 per cent. of air and also of carbonic acid, and 28 per cent. to the rate of respiration.

"Spring is the season of the greatest, and the autumn of the least activity of the respiratory and other functions."

"Temperature and atmospheric pressure only partially explain the effect of season, for with the same temperature, at different seasons, there is a great diversity in the carbonic acid expired, and particularly with a medium temperature, as for example 59°, with which the quantity of carbonic acid was 9·13 grains (in the minute) in the spring, and 6·76 grains in the summer and autumn. The relation of temperature and pressure to the carbonic acid is an inverse one, the former acting in an *increasing ratio* in cases of sudden increase."

* I regret very much that I have not been able to make more use of Dr. Smith's valuable memoirs, which I only received as these pages were going through the press. They are contained in the Philosophical Transactions for 1859, and are deserving of the highest praise for the great amount of personal experiment and research which they record.

"The period of permanent decline in the carbonic acid is May and June, and at the period of minimum quantity there is the greatest uniformity."

Moisture.

The moisture of the atmosphere exerts an influence on the respiratory functions, and especially on the excretion of carbonic acid. Lehmann found from experiments * on wood-pigeons, green-finches and rabbits, that the weight of carbonic acid excreted in moist air greatly exceeds that eliminated in a dry atmosphere. For example, 1000 grammes weight of wood-pigeons excreted 4·69 grammes of carbonic acid in one hour in *dry* air at a temperature of 98·6°, and 7·76 grammes in *moist* air at the same temperature. (At a lower temperature, *e. g.* 74°, the difference is less marked, the number of grammes being 6·06 and 6·77); similarly 1000 grammes weight of green-finches yielded in *dry* air 3·22, and in *moist* air 6·86 grammes of carbonic acid at the temperature of 99·5°; and 1000 grammes weight of rabbits yielded 0·451 of a gramme of carbonic acid in *dry* air, and 0·677 of a gramme in *moist* air at a temperature of 99·5.

Atmospheric pressure.

The influence of the pressure of the air has been investigated by Vierordt on man, and by Legallois and by Lehmann on mammals and birds. A rise of the barometer (*e. g.* an increased atmospheric pressure) renders the pulse and respiration more rapid, and increases the amount of expired air; as however the per-centage of the carbonic acid in the exhaled air is diminished, the absolute amount is not much affected. Sudden changes of pressure in either direction give rise to increased frequency of the respirations, and thus augment the quantity of carbonic acid; but if the change be gradually effected the pressure may be increased or diminished to a great extent without materially altering the amount of

* These experiments seem to have a direct bearing on the treatment of disease. When we wish to check the too rapid waste of tissue (of which the excreted carbonic acid is a measure), we should clearly recommend a dry in preference to a moist atmosphere.

carbonic acid that is exhaled in a given time. In Lehmann's experiments the animals were quite as lively and as much disposed to eat, with the barometer either at 34 or at 22 inches as at the mean pressure.

Periods of the day.

Prout was led to believe from his experiments that the different periods of the day exerted a direct influence upon the exhalation of carbonic acid. Although his experiments were doubtless made with his well-known accuracy, it is probable (as Scharling, Vierordt and Lehmann suggest) that the differences observable in the amount of carbonic acid are far more dependent upon internal conditions of the organism, such as digestion, waking and sleeping, &c. than on the special periods of the day. Marchand, who formerly held the opposite opinion, now believes that the influence of day and night are very inconsiderable, and that the slight diminution which the carbonic acid presents during the night can only be referred to the more quiet condition of the animal at that period. Moleschott found that light (independently of the period of the day) exerted, in the case of frogs, a decided influence in promoting the excretion of carbonic acid; and this fact may have a bearing on Prout's experiments.

Periods of the year.

From experiments made by Barral and Vierordt it appears that in the winter there is a greater exhalation of carbonic acid (by about one-fifth) than in the summer. Dr. Smith does not think that these observations were made with such regularity and with such identity of external conditions as to educe the true effect of season. His own observations however (see p. 468) on the whole confirm the views of Barral and Vierordt. The following are the monthly averages of the carbonic acid per minute obtained by Dr. Smith from observations upon himself: we add the mean temperature, inspired air, pulse, and respirations per minute.

| | Temperature. | Carbonic Acid. | Air. | Pulse. | Respirations. |
|---|---|---|---|---|---|
| | | Grains. | Cubic In. | | |
| April . . | 54·5 | 8·58 | 498 | 72·8 | 14·3 |
| May . . | 58·1 | 8·89 | 457 | 68·3 | 12·4 |
| June . . | 71·7 | 8·19 | 426 | 71·1 | 11·64 |
| July . . | 65·1 | 7·62 | 393 | 69·8 | 11·0 |
| August . . | 66·6 | 7·15 | 392 | 73·3 | 10·9 |
| September . | 61·2 | 7·13 | 402 | 66·6 | 10·94 |
| October . . | 52·8 | 7·67 | 395 | 69·8 | 10·93 |
| November . | 43·8 | 7·86 | 414 | 69·1 | 10·87 |
| December . | 45·2 | 8·27 | 429 | 67·0 | 11·15 |
| January . . | 43·1 | 8·35 | 447 | 68·8 | 11·73 |
| February . . | 46·3 | 8·20 | . . | 69·2 | 11·35 |
| March . . | 48·9 | 8·25 | . . | 70·9 | 11·38 |

Internal conditions of the organism.

(333.) All internal conditions of the system, and especially those which affect nutrition and consequently the state of the blood, exert a marked influence on the respiration, as starvation, digestion, &c.

Abstinence.

Numerous observers, amongst whom we may especially mention Letellier, Boussingault, Marchand, Regnault and Reiset, and Bidder and Schmidt, have carefully studied the effect of perfect abstinence (inanition) on the respiratory process. A tolerably full summary of these experiments may be found in Lehmann's "Physiological Chemistry," vol. iii. pp. 351–54; the main results being as follows. In cases of perfect abstinence from food the absorption of oxygen diminishes with tolerable constancy till death ensues, the diminution being rather more rapid at the beginning and at the close of the experiment than at the middle. In the early part of the experiment about 80% of the absorbed oxygen is expended in the formation of carbonic acid, while at the close of the experiment only 73% is thus used. The quantity of excreted carbonic acid diminishes with tolerable uniformity and rapidity during the first third of the experiment, more slowly during the second third, and again more rapidly during the last third. The quantity of aqueous vapour which is daily exhaled decreases during inanition slowly and with tolerable regularity, but the decrease is

somewhat more rapid at the beginning and end of the experiment. When water was allowed the daily amount of carbonic acid was far less considerable than when both solids and fluids were withheld. In birds and sometimes in mammals an absorption of nitrogen was observed.

Vierordt found that the omission of even a single meal considerably modifies the respiratory products, the absorption of oxygen and the excretion of carbonic acid being perceptibly diminished. His statement that there is a marked augmentation both of the absorbed oxygen and of the exhaled carbonic acid during the two hours that succeed the ingestion of a meal, has been confirmed by the observations of Scharling, Becher, and Smith; the latter found that the maximum quantity of carbonic acid was observed in from one to two hours after a meal, the increase beginning immediately after its ingestion.

Dr. Smith found that in a prolonged fast of twenty-seven hours the diminution per cent. from the quantities in a day with food, was 25 of carbonic acid, 30 of air, 37 of vapour, ·7 of rate of respiration, and 6 of rate of pulsation.

The composition of the expired air is very uniform during fasting. Dr. Smith found that at the end of the twenty-seven hours the quantity of exhaled carbonic acid was the same as at four and a half hours after the beginning of the experiment.

Influence of the chemical nature of the food.

(334.) It has been proved by various experimentalists (Dulong, Despretz, Lassaigne and Yvart, and Regnault and Reiset) that the products of respiration are essentially modified by the chemical character of the food. The most recent of these observers, Regnault and Reiset, found that a much larger quantity of oxygen was employed in the formation of carbonic acid when dogs had been fed on amylaceous substances, than when the food had been of a purely animal nature; in the latter case only 74·5 of every 100 parts of the absorbed oxygen were found again in the carbonic acid; while

in the former 91·3 parts of oxygen went to form carbonic acid. Nitrogen was eliminated during a vegetable diet, but in far less quantity than during an animal diet. In a dog which had been fed on mutton suet, only 69·4% of the absorbed oxygen was employed in the formation of carbonic acid, and nitrogen was neither exhaled nor absorbed.

We can account chemically for these differences in relation to the absorbed oxygen and the exhaled carbonic acid, if we assume (which at present we must do) that all the carbon and hydrogen of the fats and carbo-hydrates, derived from the food, are entirely oxidised in the body into carbonic acid and water. Now these substances require very different quantities of oxygen for their perfect oxidation. The mean composition of the fats is about 78·13 C, 11·64 H, and 10·13 O. The oxidation of the carbon and of the hydrogen in 100 parts of fat (into carbonic acid and water) would require 208·35 + 93·92, or 302·27 grammes of oxygen; but as the fat already contains 10·13% of oxygen, the quantity actually required is 292·14 grammes. When we compare the composition of sugar or of starch with that of fat, we see that the carbo-hydrates require far less oxygen for their complete oxidation, because, in the first place, they contain enough oxygen to oxidise their hydrogen; and secondly, because for equal weights there is far less carbon to be oxidised in the carbo-hydrates than in fat. Certain organic acids, such as tartaric and citric acids, which occur in many kinds of vegetable food, contain so large an amount of oxygen, that it not only oxidises the hydrogen but a part of the carbon. When animals are fed on nitrogenous food, we know that a portion of the carbon, hydrogen, and oxygen is carried off with the nitrogen in the form of urea, and other less abundant nitrogenous constituents which we may neglect in the present consideration. Hence we can only consider that a portion of the albuminates, and similar substances, is capable of supporting respiration, and we determine that portion by abstracting

from the composition of the albuminates, and other nitrogenous nutrient substances, an amount of urea equivalent to the quantity of nitrogen which they contain.*

It we take oxygen as our unit, and calculate how much of each of these various articles of food is required to form carbonic acid and water by combining with the unit of oxygen, we obtain what have been termed by Liebig *respiratory equivalents*, which stand in an inverse ratio to the value which each individual nutrient substance possesses for undergoing oxidation in the animal body, or (which is the same thing) for the development of animal heat. If, for instance, we assume that an organism in the full performance of its vital powers must consume about 100 grammes (or any other measure) of oxygen in a definite time, the following quantities of different articles of food would be required for the formation of carbonic acid and water, namely, 34·23 grammes of fat, 84·37 grammes of starch, 93·75 grammes of sugar, 120·80 grammes of malic acid, and 65·23 grammes of dry albuminates. The youngest student of physiology knows that no individual substance taken from this series can of itself support life; and in the next chapter we shall endeavour to determine the proportion in which they ought to be mixed, so as to form the most profitable and nourishing food. The numbers must merely be regarded as proportional estimates of the relative values of the different substances in reference to respiration.

Respiratory equivalents.

The following table gives a succinct view of these relations,

* If we abstract the sulphur, phosphorus, and salts, from the albuminates, we may regard them as composed of

| | |
|---|---|
| Carbon | 54·36 |
| Hydrogen | 7·27 |
| Nitrogen | 16·05 |
| Oxygen | 22·32 |

In urea for every 16·05 parts of nitrogen there are 6·88 of carbon, 2 29 of hydrogen, and 9·18 of oxygen. If we deduct these quantities from the corresponding quantities in the albuminates, there are left of the latter 47·18 parts of carbon, 4·98 of hydrogen, and 13·14 of oxygen, which, we must presume, are oxidised and appear in the respiratory products.

the unit now being, however, 100 parts of the nutrient substance, not 100 parts of oxygen.

| Substance. | Carbon. | Hydrogen. | Oxygen. | The quantity of oxygen required for the formation of $CO_2$ and HO, in addition to the amount already present. |
|---|---|---|---|---|
| 100 parts of fat . . . . | 78·13 | 11·74 | 10·13 | 292·14 |
| „ starch . . . | 44·45 | 6·17 | 49·38 | 118·52 |
| „ sugar ($C_{12}H_{12}O_{12}$) . | 40·40 | 6·66 | 53·34 | 106·67 |
| „ malic acid ($C_4H_2O_4$) | 41·38 | 3·45 | 55·17 | 82·78 |
| „ albuminates . . | 47·48 | 4·98 | 13·14 | 153·31 |

Dr. Smith's researches.

The recent researches of Dr. Smith have led to the following results.

1. It follows from numerous experiments that food may be divided into two classes, viz.: those which excite certain respiratory changes (excito-respiratory) and those which do not.

The excito-respiratory are nitrogenous foods, milk and its components, sugars, rum, beer, stout, the cereals and potato.

The non-exciters are starch, fat, certain alcoholic compounds, the volatile elements of wines and spirits, and coffee leaves.

2. Of the hydro-carbons, fine starch exerts but an insignificant influence over the increase of carbonic acid, and the addition of fat to starchy food lessens, rather than increases the influence of the latter; fats (olive and cod liver oil) taken alone diminish the respiratory changes; while sugar in every form is a powerful respiratory excitant.

Dr. Smith is fully aware that some of the results quoted here and in the preceding pages are not in accordance with commonly received physiological opinions, but after carefully reconsidering his labours, he finds no reason to distrust the truthfulness of his observation.

Influence of quantity of food.

(335.) The quantity as well as the quality of the food exerts a very considerable influence on the amount of the interchange of gases in the lungs. The following experiment made by C. Schmidt on a cat will sufficiently illustrate this

fact. When the animal was taking 142·41 grammes of flesh daily (a quantity which was quite sufficient to maintain its full strength and ordinary weight), it absorbed 60·14 grammes of oxygen, and exhaled 65·60 grammes of carbonic acid, together with 30·88 grammes of water; whilst during the the consumption of 247·32 grammes of flesh it absorbed 103·84 grammes of oxygen, and exhaled 113·52 grammes of carbonic acid, and 47·86 grammes of water.

Influence of alcohol, tea, &c.

(336.) Vierordt and Böcker agree with Prout in finding that the excretion of carbonic acid is both absolutely and relatively diminished even after a moderate use of alcoholic drinks. In reference to this statement Dr. Smith observes, (1) that alcohol alone was not used in the whole of Prout's and Vierordt's experiments, but various substances containing alcohol were used by the former and white wine by the latter; (2) that there is the utmost variation in the composition and quality of fluids of this kind; and (3) that there was probably great variation in the habits of some of the experimenters.

His own observations on the effects of alcohol have led to several singular and unaccountable results. The following are his chief conclusions —

1. The direct action of pure alcohol was much more to increase than to lessen the respiratory changes, and sometimes the former effect was very distinct.

2. Brandy, whisky, and gin (particularly the latter) almost always lessened the respiratory changes, whilst rum as commonly increased them. Rum and milk had a very pronounced and persistent action. Ale and porter always increased them, while sherry lessened the quantity of air inspired, but slightly increased the carbonic acid evolved.

3. The volatile elements of alcohol, gin, rum, sherry, and port, when inhaled, lessened the quantity of carbonic acid exhaled, and usually lessened the quantity of air inhaled. The effect of fine old port was very decided. The excito-

respiratory action of rum is probably not due to its volatile elements.

4. In these experiments there was no parallelism between the exhalation of vapour and of carbonic acid.

Prout, Vierordt, and Böcker, found that strong tea and coffee, like spirituous liquor, occasioned both an absolute and a relative diminution of the carbonic acid. Dr. Smith's results do not support this view. He finds from his experiments on this class of substances: —

1. That tea, coffee, chicory, and cocoa, are respiratory excitants, whilst coffee leaves depress the respiratory function.

2. Tea is the most powerful, then coffee and cocoa, and lastly, chicory.

3. The addition of an acid or alkali lessens the effect of tea.

4. The addition of sugar and milk in the ordinary way increases the effect.

5. Cold tea and tea infused and kept twenty-four hours, has as much effect as when hot and recently made.

6. The influence of both tea and coffee is exerted almost immediately, and the maximum is attained in from twenty-five to sixty minutes. The duration varies from one to two hours.

Strong tea and coffee, ethereal oils, &c., produce a similar effect.

Of sleep.

(337.) It has been shown by the experiments of Scharling on men and by those of Lehmann on birds, that sleep causes a very considerable diminution in the amount of the excreted carbonic acid. A man, who after dinner exhaled 33·69 grammes of carbonic acid in an hour, exhaled only 22·77 grammes during an hour while sleeping; in another case the ratio was 40·74 : 31·39.

Of hybernation.

The respiratory products of animals in the hybernating state (especially marmots) have been carefully studied by Regnault and Reiset. In their active state marmots, for every 1000 grammes of their bodily weight, absorb from 0·77 to

1·2 grammes of oxygen in an hour, while in their hybernating condition they consume only from 0·04 to 0·05 of a gramme. In the hybernating animals only 56·7% of the absorbed oxygen passes into carbonic acid, whilst in the active state the quantity amounts to about 73%. These observers found that the marmots when they awake from their hybernation exhale an extremely large quantity of carbonic acid and consume an excessive quantity of oxygen—an observation which corresponds with the fact, noticed both by Prout and Vierordt, that man for half an hour or nearly an hour after waking exhales an excess of carbonic acid.

Of exercise.

There is abundant evidence that bodily exercise increases both the absolute and the relative amount of carbonic acid.

Of age.

The influence of age on the respiratory products has been studied by Andral and Gavarret, who found that the quantity of carbonic acid which is daily excreted increases on an average to the fortieth or forty-fifth year, and apparently in a direct ratio with the development of the muscular system. For equal bodily weights, however, children of nine or ten years of age exhale nearly double as much carbonic acid as adults (Scharling).

Of sex.

With regard to sex, the experiments of Scharling as well as those of Andral and Gavarret show that males from childhood upwards exhale more carbonic acid than females. This influence of sex has been found to be equally well marked in man and the lower animals.

Regnault and Reiset found that lean animals consume more oxygen and exhale more carbonic acid, than very fat ones,—a result which is in accordance with the observations made by Bidder and Schmidt, that fat animals excrete far less bile than lean ones.

Tabular view of the normal relations of carbonic acid.

(338.) We may conclude this part of the subject with the following table, which is based on Scharling's observations, and which may be regarded as showing the normal numerical relations of the excreted carbonic acid.

| Subject. | Age. | Weight. | Carbonic acid exhaled in one hour. | Amount of carbonic acid exhaled in one hour for each 1000 grammes weight. |
|---|---|---|---|---|
| | Years. | Kilogrammes. | Grammes. | Grammes. |
| Man . . | 35 | 65·50 | 33·530 | 0·5119 |
| Youth . . | 16 | 57·75 | 34·280 | 0·5887 |
| Soldier . | 28 | 82·00 | 36·623 | 0·4466 |
| Girl . . | 17 | 55·75 | 25·342 | 0·4546 |
| Boy . . | 9¾ | 22·00 | 20·338 | 0·9245 |
| Girl . . | 10 | 23·00 | 19·162 | 0·8831 |

The numbers obtained by Andral and Gavarret differ slightly from Scharling's. They find, that an adult man exhales on an average from 38·5 to 40·3 grammes of carbonic acid in an hour; an adult female, when not pregnant, from 22·0 to 23·8 grammes; during pregnancy, 29·3 grammes; and after the cessation of menstruation, from 27·5 to 31·2 grammes. Although Scharling's numbers include the products of perspiration with those of respiration, they are probably (from the mode in which he conducted his experiments), the more accurate of the two.

Since the above paragraphs were written, I have received Dr. E. Smith's memoirs, which have been already referred to. After noticing the discrepant results of previous inquirers, he gives his own results obtained from experiments made upon himself and upon three friends,—all men in the prime of life, the ages being 38, 48, 26, and 33 years. The following are the total average results in 24 hours,—

| | Carbonic Acid. | | Carbon. |
|---|---|---|---|
| In quietude . . | 26·193 oz. | = | 7·144 oz. |
| With gentle exercise . | 31·824 „ | = | 8·680 „ |
| With exercise (on the treadmill) | 43·000 „ | = | 11·700 „ |

or as a general average, 33·67 oz. of carbonic acid, and 9·18 oz. of carbon. Of the 26·193 oz. expired in a state of rest, 1950 grains were expired in the six hours of the night. The proportion per minute in the night and the day is 1 to 1·84.

Respiration in animals.

(339.) The peculiarities presented by the respiratory relations in different classes of animals, may be here briefly noticed.

With reference to the mammalia, we find from the re-

searches of Regnault and Reiset (which in many respects have been confirmed by the subsequent investigations of Bidder and Schmidt), that the differences which have been observed in the respiratory relations of the herbivora and carnivora, do not depend upon any difference in their organisation, but are solely due to the influence of their food. For in the same manner as we observe that the urine of the carnivora, when fed upon vegetables, becomes similar to that of the herbivora, and that conversely the urine of the herbivora may be made, by feeding them on animal food, to resemble that of the carnivora (see p. 346), so also we find that carnivora, which are made to live principally on amylaceous matters, exhibit the same respiratory relations as the herbivora, and conversely. Carnivorous animals absorb more oxygen and exhale more carbonic acid and nitrogen than herbivorous animals.

The respiratory activity is very different in different kinds of birds; small singing birds, which are constantly flying about and always in a state of activity except when asleep, consuming ten times as much oxygen, and exhaling nearly ten times as much carbonic acid (weight for weight), as the common hen, which seldom flies, and consumes little more oxygen than rabbits, and less than dogs. These differences are clearly brought out in the following table, which is based upon Regnault and Reiset's observations. (The small birds were green-finches, cross-bills, and sparrows, and the numbers are mean results.)

| Animals. | Food. | Of 100 parts of absorbed oxygen there pass into the carbonic acid | For 1000 grammes weight in one hour | | |
|---|---|---|---|---|---|
| | | | Consumed oxygen | Exhaled carbonic acid | Exhaled nitrogen |
| | Oats. | | grammes. | grammes. | grammes. |
| Hens . . . | Moderately | 87·7 | 1·053 | 1·320 | 0·0079 |
| Small birds . | Sparingly | 75·3 | 11·473 | 11·879 | 0·1296 |

During incubation, the eggs of birds exhale carbonic acid,

and absorb more oxygen than is contained in the exhaled carbonic acid; and in proportion as the embryo becomes more fully developed, a larger amount of oxygen is absorbed from the air, and more carbonic acid given back to it. Even in fresh, unincubated eggs, a similar change takes place, although in a less marked degree. In eggs.

It is unnecessary to state more regarding the respiration of reptiles and amphibians, than that (as might have been assumed *à priori*), the interchange of gases in the lungs is most abundant in those of most active habits. The lizard, for example, absorbs more than twice as much oxygen as the frog, weight for weight. The respiratory process is on the whole far less energetic in these animals than in mammals or birds. In reptiles and amphibians.

The respiration of gill-breathing animals (fishes, crustaceans, &c.) has not been investigated in its general bearings by any recent chemist; indeed, almost all that we know regarding the respiratory products of fishes (excepting in relation to one or two special points) is due to Humboldt and Provençal. They ascertained that the oxygen which is absorbed exceeds that which is exhaled in the form of carbonic acid (the latter amounting to scarcely four-fifths, and often to only half the former); that nitrogen is constantly absorbed in large quantity, and that fishes, like other animals, transpire copiously through the skin. They likewise ascertained that fishes are capable of breathing in atmospheric air as long as their gills are kept moist, the products of respiration being the same as when they are breathing in water, which is a proof that respiration in these water-breathing animals follows the same laws as those which control atmospheric respiration: Baumert has shown that in active fishes (like the gold-fish) the interchange of gases is far more energetic than in sluggish fishes (like the loach). He has likewise investigated the respiratory products of the pond-loach, a fish, which, in addition to its branchical respiration, possesses an intestinal respiration, as In fishes.

was shown many years ago by Ermann. He found that the air which was eliminated through the intestinal canal contained much less oxygen than the air which the fishes had swallowed; the oxygen had however been replaced by much less carbonic acid than we usually meet with in branchial or pulmonary respiration. Hence, while the oxygen which is absorbed by the intestine passes into the blood, the carbonic acid to which it gives rise is not eliminated by the intestine but by the gills, and consequently these fishes exhale an excess of carbonic acid as compared with the oxygen which they absorb from the water.

The respiratory products of insects in their different phases of metamorphosis have been especially studied by Regnault and Reiset, and by Lehmann. The variations in the degree of animation in the motions of insects produce remarkable differences in the quantity of carbonic acid which they excrete; and on that account, probably, the pupa exhales only 1-190th or 1-160th part of the carbonic acid which is exhaled by the more active caterpillar, weight for weight.

Of animals possessing no special organs of respiration the earth-worm is the only one which has been made the subject of special investigation. Regnault and Reiset prove that the respiration of this animal is very similar to that of the frog, which (in addition to its pulmonary respiration) breathes vigorously through its skin. They ascertained that one kilogramme weight of these animals absorbed, in one hour, 0·1013 of a gramme of oxygen, and exhaled 0·0982 of a gramme of carbonic acid; the absorbed oxygen being to the oxygen contained in the expired carbonic acid in the ratio of 100 to 77·5.

The following tabular view of the respiratory relations of different classes of animals has been drawn up by Lehmann.

| Animal. | Food. | Proportion of absorbed oxygen in 100 parts of carbonic acid. | For 1000 parts (by weight) of the animal in one hour. | | |
|---|---|---|---|---|---|
| | | | Absorbed oxygen. | Exhaled carbonic acid. | Exhaled nitrogen. |
| Dogs . . . | Flesh | 74·5 | 1·183 | 1·211 | 0·0078 |
| Rabbits . . | Turnips. | 91·9 | 0·883 | 1·116 | 0·0036 |
| Hens . . . | Oats. | 80·7 | 1·053 | 1·320 | 0·0079 |
| Small birds . | Oats. | 75·3 | 11·473 | 11·879 | 0·1296 |
| Frogs. . . | | 76·0 | 0·084 | 0·088 | 0·0005 |
| Newts . . | | 82·4 | 0·085 | 0·096 | |
| Lizards . . | | 75·2 | 0·192 | 0·198 | 0·0025 |
| Cockchafers . | | 80·8 | 0·0195 | 1·1372 | |
| Silk-worm moths | | 78·2 | 0·899 | 0·960 | |
| Tenches . . | | 72·3 | 0·0143 | 0·0138 | |
| Gold-fish . . | | 72·3 | 0·0409 | 0·0419 | |
| Earth-worms . | | 77·5 | 0·1013 | 0·0982 | |

In all these experiments the exhalations from the skin are included with those of the lungs; the carbonic acid exhaled from the skin has however been shown by special observations of Regnault and Reiset to be very trifling as compared with that from the lungs, both in mammals and birds, and seldom to amount to 1-50th of the whole carbonic acid: but in the amphibia this is by no means the case; frogs in which the lungs have been extirpated not only living for a long time, but yielding almost as much carbonic acid and aqueous vapour as if they had been uninjured.

Respiration in disease.

(340.) Notwithstanding the investigations of Scharling, Hannover, and other inquirers, our knowledge of the effects of different diseases upon the respiratory products is still so very deficient and indefinite, that it seems advisable to pass the subject entirely over with the remark, that those who wish to investigate it will find a full account of all the experiments that have been made regarding it in the third volume of Lehmann's Physiological Chemistry, pp. 376—382.

Origin of the carbonic acid.

(341.) We shall conclude this chapter with a few remarks upon the origin of the carbonic acid, and on the theory of animal heat. We have already shown in different parts of this volume, that various gases (carbonic acid, oxygen, and nitrogen) are present, not only in the blood but in the

lymph, chyle, and indeed in all the fluids of the body; and Lehmann has demonstrated by positive experiments that there is not a single vital organ in the whole organism from which we may not with the air-pump extract free carbonic acid, nitrogen, and some traces of oxygen. The carbonic acid is, at all events for the most part, formed by the individual organs and tissues in the exercise of their respective functions, and is not primarily evolved in the blood. In insects this is obviously the case, for in this class of animals there is no true blood, nor (excepting the dorsal vessel) are there any true blood-vessels; the air comes directly in contact, through the stigmata and tracheal ramifications, with every portion of the tissues of the different organs; and as the experiments of Newport and others show us that the amount of excreted carbonic acid rises and falls in direct proportion to the activity of the insects, it is clear that this gas must be formed in the parenchyma of the organs themselves, and through their vital energy. This fact alone would render it extremely probable that in the higher animals also the greater portion of the carbonic acid is likewise formed in the various organs, and not in the blood. But independently of probability, we have direct proof that this is the case in the investigations of G. Liebig, to which we have already referred (see p. 405). He has distinctly proved that carefully prepared frogs' muscles absorb oxygen and exhale carbonic acid so long as their irritability lasts, that the latter is lost in irrespirable gases, and finally that a muscle completely deprived of blood continues to maintain this interchange of gases so long as it retains its contractility. Here then we have a true respiration taking place in a higher animal, without blood and without special air-passages. As, moreover, these experiments show that the muscles require the free access of oxygen in order to preserve their contractility, it is clear that a large portion of this gas, after being absorbed by the lungs, must be conveyed in a free state through the blood and the walls of the capillaries into the muscles; and consequently the blood serves the

double purpose, of conveying to the muscles the amount of oxygen necessary for the performance of their functions, and of carrying back the carbonic acid formed by this function; and we have an interchange of gases — in short, a respiratory act — taking place in the tissues of the organs between the parenchymatous juice and the blood in the capillaries.

We must not, however, conclude from the preceding observations, that the whole of the carbonic acid is formed in the tissues of the organs. Previously to Harley's and to Meyer's investigations (see note, p. 220), which have placed the matter beyond all doubt, there were strong reasons for believing that a part of the oxygen which is absorbed in the lungs enters into chemical combinations while in the arterial blood. We know, for example, that oxygen is absorbed by the blood in far greater quantity than we should have expected from the ordinary laws of absorption (see p. 220); that the absorption of oxygen by the blood is not dependent on external pressure, as would be the case if it were merely mechanical; that the modifications which the blood undergoes in its passage through the pulmonary capillaries, after it has given off its carbonic acid and absorbed oxygen, must be referred to chemical changes in some of its constituents (see p. 219); and lastly, that hæmatin and hæmatocrystallin possess the property of combining readily with oxygen (see pp. 95 and 215). The fact that acetate or tartrate of potash or soda (or any vegetable salt of this class) when injected into the veins, becomes rapidly oxidised and reappears in the urine as a carbonate, indicates that a certain portion of carbonic acid is formed in the arterial blood; and it is probable that many other substances are similarly acted upon in the circulating fluid.*

(342.) The subject of Animal Heat is usually associated with that of respiration. Animal heat must not, however, be re- Animal heat.

* For further information on the subject of this paragraph, I may refer the cader to a paper by Dr. E. Smith, "On the Immediate Source of the Carbon exhaled by the Lungs," published in the Philosophical Magazine for December 1859.

garded as a direct consequence of respiration, as was supposed by Lavoisier and his followers, inasmuch as it is not specially engendered in the lungs, but is for the most part the result of the general oxidation which is going on through the tissues in all parts of the body.

We are indebted to G. v. Liebig for the discovery of the remarkable fact (which has since been independently confirmed by Bernard and Walfarden), that so far from the lungs being the chief seat of the production of heat, the blood is actually cooled in passing through those organs, and is about 0·2° lower in temperature in the left, than in the right side of the heart. As a certain amount of latent heat must be liberated by the absorption of oxygen in the lungs, the result must be explained by this augmentation of temperature being more than balanced by the exhalation of carbonic acid and aqueous vapour.

Direct experiments, made with the object of comparing the amount of animal heat with the heating power of different kinds of food, show that at least one-twentieth of the heat developed by an animal cannot be referred to the oxidation or combustion of the food; or, in other words, the oxidation of the food cannot, so far as we at present know, produce more than nineteen-twentieths of the actual heat.* Future investigations will probably clear up this discrepancy. The small deficiency, which is still unaccounted for, may be made up by the heat, which (as we learn from the thermo-electric investigations of Becquerel and Breschet, and of Helmholtz) is developed by the muscles during their contraction. There is also reason to believe that all nervous action is accompanied by a slight development of heat.

* I quote these numbers on the authority of Lehmann (Handbuch d. Phys. Chem. 2nd Ed. 1859, p. 385), but do not know how or by whom they were obtained. Despretz found that in carnivorous animals (cats and dogs), from 76 to 80% of the animal heat might be referred to the oxidation (or combustion) of the carbon and hydrogen of the food, while in herbivorous animals (rabbits and guinea-pigs), the corresponding numbers were 86—88%, in carnivorous birds 75%, and in granivorous birds 79%.

# CHAPTER XX.

## NUTRITION.

Investigations preliminary to that of nutrition.

(343.) The study of the process of nutrition must be regarded as constituting the true ultimate aim of all physiologico-chemical inquiries. In the preceding pages we began by considering the various organic and inorganic bodies of which the living organism is composed, or which are formed within it—the organic substrata, as Lehmann terms them; we then noticed the various fluids of the body, and the parts which both the solids and fluids perform in the accomplishment of the most essential functions of animal life; and we have endeavoured to determine the uses or functions of the four great groups — the protein-bodies, the fats, the carbo-hydrates, and the mineral matters, within the animal organism. If we have been successful in this endeavour, the reader will at once perceive that these four essential adjuncts in the metamorphosis of the animal body must also be contained in those articles of food which are required for the renovation and restoration of those particles which have been lost or worn out, and for the due accomplishment of the vital phenomena.

Necessity of an admixture of the different kinds of food in certain proportions.

(344.) It is only comparatively recently that we have learned from French and Dutch gelatin commissions, and from numerous independent observations on animals, that in order to supply the wants of the system food must consist of a combination of these four groups, and that animals which are fed exclusively on food belonging to one of the groups, as for instance albumen or fibrin, perish under symptoms of inanition exactly as if they had been deprived of all nourish-

ment.* As in the milk destined for the infant we find representatives of each group in the casein, butter, sugar, and various salts, so, for other periods of life, these nutrient matters, whether derived from the animal or the vegetable kingdom, must contain a due admixture of the four types; and in considering the nutritive value of any article of food in any special case, we must further bear in mind that it not only depends upon the proportion in which the four fundamental groups are combined, but also in part upon the indi-

* The researches of Dr. Hammond (see pp. 341–42), "On the nutritive value and physiological effects of albumen, starch, and gum, when singly and exclusively used as food," are so important, that although they prove more than the mere statement that an admixture of the different groups of food is necessary for the well-being of the animal economy, I give them here with little abridgement.

"1. Albumen may be assimilated into the system in such quantity as to furnish a sufficiency of both nitrogen and carbon to the organism.

2. Under the use of an exclusively albuminous diet the nitrogenous constituents of the urine are increased over the ordinary average amount, though not in proportion to the quantity of albumen absorbed into the circulation.

3. Either some other means than the urine exist for the elimination of nitrogen from the system, or the excess (over two-thirds) is retained in the organism even when the body is rapidly decreasing in weight.

4. The continual use of albumen as an article of food increases the proportion of this substance (and of fibrin) in the blood, and in a short time causes it to appear in the urine.

5. Whilst pure albumen cannot be regarded as of itself adequate to supply the several wants of the system, there is no reason why, when associated with suitable inorganic matters, it should not support both life and health. [I think this statement is open to grave doubt.]

6. Starch may be assimilated by the absorbents in more than sufficient quantity to sustain the respiratory function.

7. Under its use the nitrogenous constituents of the urine are very much reduced in amount, even below what would probably occur during inanition; and although starch is not capable of nourishing the tissues, it is yet serviceable, independently of its heat-producing power, in retarding their destructive metamorphosis.

8. The continued use of highly amylaceous food causes the appearance of sugar in the urine.

9. Under the use of such aliments, the nitrogenous constituents of the blood are diminished, and the carbonaceous increased.

10. Gum is altogether incapable of assimilation, and therefore possesses no calorifacient or nutritive power whatever, but is, on the contrary, a source of irritation to the digestive organs."

vidual requirements of the organism that is to be nourished, and that it may thus vary with age, amount of bodily exercise, &c., or in the case of domestic animals, with the object that we have in view in feeding, whether, for instance, we are training an animal for feats of speed or strength, whether we are fattening it for the market, or whether we are endeavouring to increase its quantity of milk.

Digestibility as an element of the nutritive value.

(345.) In judging of the nutritive value of any kind of food we must not overlook its digestibility. It is well known that hard-boiled eggs, meat that has been boiled for a long time, and hard cheese which is poor in fat and in salts, are less easily digested than soft-boiled or fresh eggs, meat steeped in vinegar, or moist fat cheese; and that starch is much more readily converted into sugar when boiled than in the raw form. Hence articles of food of the same chemical composition may have very different nutritive values.

Nitrogen as a measure of the nutrient value.

(346.) As the nitrogenous constituents of the food (the articles of food containing albumen, fibrin, casein, &c.) are principally employed in the formation of the blood and the reproduction of the tissues, it was at one time thought that the quantity of nitrogen which any kind of food contained might be taken as a measure of its nutritive value; and almost all the ordinary kinds of food have consequently been analysed with special reference to this constituent. Boussingault has determined the per-centage of nitrogen in almost all the vegetables commonly used as human food; R. Dundas Thomson has similarly analysed different varieties of bread and flour; Schlossberger and Döpping have done the same for the fungi; while Schlossberger and Kemp have made similar observations on an enormous number of animal substances (including the flesh both raw and cooked of mammals, birds, fishes, crustaceans, and mollusks, eggs, varieties of milk and cheese, &c.) The results of these investigators are given in detail in Lehmann's Physiological Chemistry vol. iii. pp. 401—403. One of the most important of the conclusions to

be drawn from these investigations is that the amount of nitrogen in muscular fibre does not essentially differ throughout the whole animal kingdom, the average per-centage of nitrogen being about 13.

We cannot however judge directly from the amount of its nitrogen regarding the nutrient value of any kind of food in reference to the formation of blood and tissues, for the nitrogen which is found depends in part upon the gelatigenous matters, which probably contribute little or nothing to the reproduction of the tissues.

In addition to the nitrogen-analyses to which we have already referred, we must mention that at Liebig's suggestion Horsford analysed a large number of varieties of vegetable food, in reference not only to their per-centage of nitrogen, but also to that of their sulphur, ash, albuminous substances, non-nitrogenous ingredients, and water; and as his non-nitrogenous ingredients contain not only starch, but cellulose, wax, &c., Krocker made a similar set of observations in reference to the actual per-centage of starch, and from these and some other determinations Liebig has constructed a table which affords a general view of the proportion between the albuminates and the non-nitrogenous nutrient substances (fat, starch, and sugar) occurring in the most common articles of human food (10 parts of the albuminates being taken as the unit of comparison). As the non-nitrogenous matters exert a different influence on the generation of heat, according as they are fats or carbo-hydrates, we take their respective amounts of oxygen as the measure of comparison between them. In this way 10 parts of fat correspond, in reference to the generation of heat, to about 24 parts of starch, and sugar of milk and glycose are obviously reduced to the corresponding value of starch by the deduction of a certain quantity of water. On this supposition (that is to say, reckoning all the non-nitrogenous constituents as if they were solely starch) the ratio of the plastic to the non-nitrogenous

constituents of food is as follows in the different articles in the subjacent table:

| | Plastic. | Non-nitrogenous (Calculated as starch). | |
|---|---|---|---|
| In Cows' milk . | 10 | 30 | = { 8·8 fat, 10·4 milk-sugar |
| „ Woman's milk | 10 | 40 | |
| „ Lentils . . | 10 | 21 | |
| „ Horse beans . | 10 | 22 | |
| „ Peas . . | 10 | 23 | |
| „ Fat mutton . | 10 | 27 | |
| „ Fat pork . | 10 | 30 | |
| „ Beef . . | 10 | 17 | |
| „ Hare . . | 10 | 2 | |
| „ Veal . . | 10 | 1 | |
| „ Wheat-flour . | 10 | 46 | |
| „ Oat-meal . | 10 | 50 | |
| „ Rye-meal . | 10 | 57 | |
| „ Barley . . | 10 | 57 | |
| „ White potatoes | 10 | 86 | |
| „ Blue „ | 10 | 115 | |
| „ Rice . . | 10 | 123 | |
| „ Buckwheat-meal | 10 | 130 | |

Ratio of the plastic to the non-nitrogenous constituents of food.

(347.) Both every-day experience and chemico-physiological observations show us that the best kind of food must contain fat as well as carbo-hydrates. We have seen that under favourable conditions the animal body is able to form fat from the carbo-hydrates, but this production of fat seems to be limited; and further, we have shown that fat and sugar fulfil distinct objects in the animal economy. Instinct teaches us to combine highly amylaceous foods with fats (as for example bread and butter, beans and fat bacon); and the increased digestibility of such mixtures proves, no less than the simultaneous occurrence of fat and sugar in the milk (the normal type of food), that both substances are necessary as independent ingredients of food: and even if one of these sub-

The best relative admixture of the different groups of food.

stances may serve (as for instance in the development of heat) as a substitute for the other, this does not in any way militate against the special utility of either. A series of accurate experiments on the proportion in which the four great nutrient groups should be combined, so as to form the food best suited to the general want of the organism, is still a *desideratum*. During the period of early life, when growth is most rapid, we may fairly infer that woman's milk presents the most suitable mixture, and in this fluid we find 10 parts of plastic matter (casein) combined with 10 parts of fat (butter), 20 parts of a carbo-hydrate (sugar), and 0·6 of a part of salts.

Various experiments show that in order that an animal should be properly nourished, its food must contain an admixture of the four great groups; in short that unless these groups are combined life cannot be supported. Thus, for instance, Letellier found that when turtle-doves were fed solely on protein-substances and sugar they gradually succumbed under the same symptoms as would have occurred if they had been deprived of all solid food. If all the different groups are present in the food, and one of them should preponderate greatly over the others, nutrition will not go on properly, as Boussingault ascertained on attempting to feed a cow on potatoes and beet-root alone.

It must further be borne in mind, that there is no single fixed proportion of the four groups suitable for all conditions of life, even in the same individual. The proportions vary in the infant, the young child, and in the adult; and (to a far greater extent) in different kinds of animals. The experiments of Crusius * show that in the cow the nutritive value of the milk is very different during different periods of lactation; and Becquerel and Vernois (see p. 281) recognise similar differences in human milk.

We have seen that cows' milk contains relatively less sugar

* Journ. f. prakt. Ch. vol. lxviii. pp. 1—23.

and more fat and casein than woman's milk; that asses' milk contains very little casein but much sugar and far more fat; and that bitches' milk contains an excess of casein with mere traces of sugar. There can then be no doubt that the requirements of the animal organism must present differences in the admixture of the nutrient matters, but at present we are quite unable to calculate with exactness the composition of the food which is best adapted for each special organism.

The necessary quantity of food.

(348.) We are better prepared to answer the following question, What are the absolute quantities of food which are requisite for the maintenance of life, and for the energetic accomplishment of all its functions? There are two methods by which we may determine the necessary amount of food. The first consists in experimenting on oneself or upon animals with the smallest possible quantities of differently mixed food, until we have been able to find the suitable amount and the most correct proportions for each individual case,—a troublesome and unsatisfactory mode of proceeding. The second is based on the investigation and quantitative determination of the excretions. If these afford a standard measure of the metamorphosis of animal matter, and if we are able, from their quantity and composition, to judge of the daily loss which the animal body experiences, they ought to give us the quantity and (to a certain degree) the chemical composition of those substances which the organism requires for the restoration of its effete matters. In order to deduce trustworthy results from this method, we must be careful to see that the organism on which we are experimenting remains at a constant weight, and in all respects maintains its normal state. By cutting off all supplies from without, and then determining the quantities of matter lost by the several excretions, we can calculate the minimum of food necessary for the support of life, which is, however, very different from the quantity which is necessary to maintain the animal in perfect health and in the full use of its powers.

The determination of the latter quantity is beset with difficulties. If the absorption of digested matters were more limited than it really is, and if no more nutrient matters entered the blood than were necessary for the wants of the system, we might perhaps make a calculation of the required quantity from a comparison of the excretions and of the food which had passed unchanged with the fæces. Now we know that the organism is not able to convert an unlimited quantity of nutrient matter into blood. The experiments of Boussingault, Bidder and Schmidt, and von Becker show that only definite quantities of fat, albuminates, or sugar can be absorbed from the intestine in a given time. But though there is a limit, it is a comparatively wide one, and numerous experiments show that a much larger amount of nutrient matter or chyle may be absorbed than is required for the reparation of lost matter or for the accomplishment of the different purposes of life. The excess that is thus absorbed enters as superfluous matter into the blood, where it is not employed either for the restoration of lost materials or for the increase of mass of the body, or indeed for the accomplishment of any apparent object, but is again given off to the external world after having undergone certain changes which facilitate its excretion. To this excessive quantity of food, much of which is superfluously absorbed, Schmidt has applied the phrase, *Luxus-consumption*. The great difficulty consists in our being unable accurately to determine the mean which will give the organism neither too little nor too much nourishment for the due performance of its various functions; and even this mean must obviously be liable to great variations in the same individual, corresponding with the degree of muscular and nervous energy.

The first of the two methods for determining the necessary quantity of food gives safe practical results, provided we make a sufficient number of observations and apply the method of statistics. We are indebted to Dr. Lyon Playfair for much

useful information on the point. The following examples of dietaries are extracted from a table attached to his memoir, "On the food of man under different conditions of age and employment." * Playfair's researches.

| | Weight of food in ounces per week. | Weight of nitrogenous ingredients. | Weight of non-nitrogenous substances. | Weight of mineral matters. | Weight of carbon. | Proportion between | |
|---|---|---|---|---|---|---|---|
| | | | | | | Carbon in flesh-formers. | Carbon in heat-givers. |
| DIETARIES OF SOLDIERS AND SAILORS. | | | | | | | |
| English soldier . . . | 378 | 36·15 | 127·18 | 4·92 | 71·68 | 1 | 3·66 |
| „ in India . . . | 261 | 34·15 | 103·19 | 2·39 | 66·32 | 1 | 3·58 |
| English sailor (fresh meat) | 302 | 34·82 | 102·89 | 3·17 | 70·55 | 1 | 3·70 |
| „ (salt meat) . | 290 | 40·83 | 132·20 | 6·03 | 87·40 | 1 | 3·94 |
| French soldier . . . | 347 | 33·24 | 127·76 | 4·62 | 85·25 | 1 | 4·72 |
| DIETARIES OF THE YOUNG. | | | | | | | |
| Christ's Hospital, Hertford | 216 | 17·16 | 61·27 | 2·47 | 39·18 | 1 | 4·21 |
| „ „ London | 242 | 17·27 | 76·82 | 2·84 | 46·95 | 1 | 5·02 |
| Chelsea Hosp., Boys' school | 245 | 12·89 | 93·28 | 5·93 | 57·67 | 1 | 8·29 |
| DIETARIES OF THE AGED. | | | | | | | |
| Greenwich pensioners . | 269 | 24·46 | 122·21 | 3·54 | 72·43 | 1 | 5·46 |
| Chelsea pensioners . . | 332 | 29·95 | 112·64 | 4·65 | 78·03 | 1 | 4·80 |
| OLD PAUPER DIETARIES. | | | | | | | |
| St. Cuthbert's, Edinburgh . | 175 | 14·80 | 89·37 | 3·31 | 46·98 | 1 | 5·85 |
| City Workhouse „ . | 107 | 13·30 | 49·99 | 1·74 | 31·48 | 1 | 4·36 |
| ENGLISH PRISON DIETARIES. | | | | | | | |
| Class 2†, males . . . | 206⅛ | 15·28 | 111·85 | 3·46 | 59·23 | 1 | 7·13 |
| „ 5‡, „ . . . | 326 | 20·29 | 130·57 | 4·23 | 73·31 | 1 | 6·65 |
| BENGAL PRISON DIETARIES. | | | | | | | |
| Non-labouring convicts . | 224 | 18·43 | 163·16 | 2·08 | 76·35 | 1 | 7·62 |
| Working convicts . . | 296 | 28·16 | 191·12 | 2·97 | 91·07 | 1 | 5·96 |
| Contractor's insuffic. diet . | 167½ | 12·70 | 135·95 | 1·30 | 61·33 | 1 | 8·88 |
| BOMBAY PRISON DIETARIES. | | | | | | | |
| Prisoners not on hard labour | 182 | 28·00 | 101·50 | 2·03 | 68·81 | 1 | 4·52 |
| „ on hard labour . | 224 | 35·63 | 128·80 | 2·45 | 87·22 | 1 | 4·50 |

From the table from which we have extracted these examples, Dr. Playfair draws the following conclusions: "Taking the soldier and sailor as illustrating healthy adult men, they consumed weekly about 35 ounces of flesh-formers, and 70—74 ounces of carbon; the relation of the carbon in the flesh-formers to that in the heat-givers being 1 to 3·6. If the dietaries of the aged are contrasted with this, it is found that they consume less flesh-formers (25—30 ounces), but rather more heat-givers (72—78 ounces); the relation of the carbon

* Edin. New Philos. Journal, 1854, vol. lvi. p. 262. I may also refer the reader to papers upon Prison and other Dietaries by Dr. E. Smith, in "The Transactions of the Society for the Promotion of Social Science, 1858," and elsewhere.

† Convicted prisoners, exceeding 7 days, but not exceeding 21 days.

‡ Convicted prisoners, hard labour, for terms exceeding 4 months.

in the former to that in the latter being about 1 to 5. The young boy, about ten or twelve years of age, consumed about 17 ounces weekly, or about half the flesh-formers of the adult man, the carbon being about 58 ounces weekly, and the relations of the two carbons being nearly 1 to 5·5. The circumstances under which persons are placed influence these proportions considerably. In workhouses and prisons the warmth renders less necessary a large amount of food-fuel to the body; while the relative amount of labour determines the greater or less amount of flesh-formers. Accordingly it is observed that the latter are increased to prisoners exposed to hard labour. From the quantity of flesh-formers in food, we may estimate approximatively the rate of change in the body. A man weighing 140lb. has about 4lb. of flesh [or rather of matter equivalent to flesh] in the blood, 27½lb. in his muscular substances, &c. and about 5lb. of nitrogenous matter in the bones. These 37lb. would be received in food in about eighteen weeks; or, in other words, that period might represent the time required for the change of the tissues, if all changed with equal rapidity, which is, however, not at all probable. All the carbon taken as food is not burned in the body, part of it being excreted with the waste matter. Supposing the respirations to be 18 per minute, a man expires about 8·59 oz. of carbon daily, the remainder of the carbon appearing in the excreted matter."

Vierordt's conclusions.

According to Vierordt*, an adult male, to keep in good condition, should take 120 grammes (or about 4 ounces) of albuminous matters, 90 grammes (or nearly 3 ounces) of fat, and 330 grammes (or about 10½ ounces) of amylaceous food daily: the non-nitrogenous being to the nitrogenous food in the ratio of 3·5 to 1. In addition to the above, there are daily ingested about 32 grammes (or about 1 ounce) of salts, about 2700 grammes (or about 84 ounces) of water, and 744 grammes (or about 23 ounces) of oxygen (in respiration).

* See his Grundriss der Physiologie des Menschen. 1860, p. 122.

(349.) Boussingault has made a series of experiments on ducks, which have a certain bearing upon an important factor in the food question. He endeavoured to ascertain in the case of these animals how much of various kinds of food they were capable of absorbing in one hour. A tolerably full account of the experiments may be found in the third volume of Lehmann's Physiological Chemistry, pp. 412—414. From them it follows that the different kinds of nutrient matter are absorbed in very different ratios. Taking the protein-matters as the unit, they stand thus,

| | |
|---|---|
| Protein-matters | 100 |
| Gelatin | 336 |
| Fat | 65 |
| Starch | 401 |
| Sugar | 429 |

Lehmann states that, from other experiments, made upon several kinds of animals, we may infer that for 1000 parts' weight of the animal, there may be absorbed in one hour,

| | |
|---|---|
| Protein-matters. | 0·710 |
| Fat | 0·465 |
| Sugar | 4·500 |

(350.) The influence of different kinds of food upon the blood (in the case of dogs), has been carefully studied by H. Nasse, who has arrived at the following results: —

Influence of the food on the composition of the blood.

1. After a purely animal diet, the blood-corpuscles exhibit a greater capacity for sinking; the blood itself presents a darker colour, which becomes whitish after the abundant use of fat; the coagulation occurs somewhat more rapidly than on a vegetable diet, and a continuous animal diet increases the amount of fibrin, (as Lehmann also observed in his own case after living exclusively on animal food,) and augments the amount of the phosphates and of the salts generally.

2. Fatty food increases the quantity of fat in the blood,

even in the course of an hour after it has been taken, but the excess rapidly disappears; and the prolonged use of fatty food does not seem persistently to increase the fat in the blood.

3. The blood is of a somewhat lighter shade of colour when the animals are kept upon vegetable food, and the sinking capacity of the corpuscles is somewhat smaller; the amount of fibrin is not altered; the fats and the phosphates are somewhat diminished.

4. After each meal the quantity of the solid constituents of the blood increases to the ninth hour, when it again begins to sink.

5. Continuous deprivation of food renders the blood somewhat pale in colour, retards its coagulation, and raises the specific gravity both of the blood generally and of the serum; the fibrin is slightly and the salts are much increased.

Distribution of the final products of the food in the excretions.

(351.) The next point we must attempt to decide is, regarding the manner in which the final products of the nutrient matter that has served its purpose in the animal economy, are distributed in the excretions. Although this subject has been studied by several excellent observers, amongst whom we may especially mention Barral, Valentin, Boussingault, and Bidder and Schmidt, the fact that their experiments have been made on very different kinds of animals, living on various kinds of food, taken in various quantities, prevents us from arriving at any definite conclusions, at all events regarding man. The very different nature of the food of carnivorous and herbivorous animals is in itself a sufficient reason for a want of uniformity in the final products: in the carnivora, for example, a much larger proportion of the fuel-products of the food passes off by the urine and the transpiration than in the herbivora, in consequence of the latter always passing a large quantity of the food from the intestine in an imperfectly digested state.

Our limited space will not allow of our noticing in detail

the experiments to which we have alluded, and we must content ourselves with three illustrations; the first showing the elements of 100 parts of the food consumed by a horse and distributed in the excretions; the second showing the same relations in the cow; and the third showing the corresponding relations in the case of a purely carnivorous animal, the cat. For the first two of these investigations we are indebted to Valentin and Boussingault, and for the third to Bidder and Schmidt. The horse and cow had their ordinary quantity of food, and the cat had for a week as much flesh as it would eat.*

* Since writing the above lines, I have met with the following instructive tables drawn up by Vierordt (Physiol. p. 192), in reference to the ultimate composition of the *ingesta* and *egesta* of man, his data being drawn from various trustworthy sources, especially from recent observations by Volz (which I have not had an opportunity of consulting.) The gramme is the unit in the following tables: and the oxygen and hydrogen of the amylaceous food are calculated as water.

*Daily Ingesta.*

| | Total. | Water. | C. | H. | N. | O. |
|---|---|---|---|---|---|---|
| Atmospheric oxygen . . | 744·11 | — | — | — | — | 744·11 |
| Albuminous food . . . | 120 | — | 64·18 | 8·60 | 18·88 | 28·34 |
| Fatty food . . . . | 90 | — | 70·20 | 10·26 | — | 9·54 |
| Amylaceous food . . . | 330 | 183·18 | 146·82 | — | — | — |
| Water . . . . . | 2635 | — | — | — | — | — |
| Salts . . . . . | 32 | — | — | — | — | — |
| | 3951 | 183·18 | 281·20 | 18·86 | 18·88 | 781·99 |

*Daily Egesta.*

| | otal. | Water. | C. | H. | N. | O. | Salts. |
|---|---|---|---|---|---|---|---|
| Respiratory products - | 229·9 | 330 | 248·8 | — | ? | 651·15 | — |
| Cutaneous products - | 669·8 | 660 | 2·6 | — | — | 7·2 | — |
| Urine . . . | 1766·0 | 178 | 9·8 | 3·3 | 15·8 | 11·1 | 26 |
| Fæces . . . | 172·0 | 128 | 20·0 | 3·0 | 3·0 | 12·0 | 6 |
| | 3837·7 | 2818 | 281·2 | 6·3 | 18·8 | 681·45 | 32 |

Comparing the H and O in the two tables, it appears that the difference of the H in the two cases, viz. 12·56, must be oxidised and converted into water, for which 100·6 of O is requisite (most of which is yielded by the atmosphere, and the remainder from the oxygen of the food). In this way, 113·1 of water is formed, which, added to the total 3837·7 makes 3950·8, which closely accords with the total *ingesta*.

In the horse:—

| Constituents of food. | Fæces. | Urine. | Respiration and Perspiration. |
|---|---|---|---|
| Water . . | 61·8 per cent. | 5·9 per cent. | 32·3 per cent. |
| Carbon . . | 34·6 „ | 2·7 „ | 62·7 „ |
| Hydrogen . . | 40·3 „ | 2·5 „ | 57·2 „ |
| Nitrogen . . | 55·7 „ | 27·1 „ | 17·2 „ |
| Oxygen . . | 41·4 „ | 1·0 „ | 57·6 „ |
| Ash . . . | 85·5 „ | 16·2 „ | — |
| The food generally | 55·3 „ | 5·2 „ | 39·5 „ |

In the cow:—

| Constituents of food. | Milk. | Fæces. | Urine. | Respiration and Perspiration. |
|---|---|---|---|---|
| | per cent. | per cent. | per cent. | per cent. |
| Water . . | 10·2 | 34·4 | 10·0 | 45·8 |
| Carbon . . | 13·0 | 25·8 | 5·4 | 54·2 |
| Hydrogen . . | 16·6 | 34·9 | 4·2 | 35·7 |
| Nitrogen . . | 22·8 | 45·6 | 18·1 | 13·5 |
| Oxygen . . | 7·9 | 37·4 | 6·3 | 48·5 |
| Ash . . . | 6·1 | 53·9 | 43·1 | 3·1 |
| The food generally | 10·3 | 34·4 | 9·9 | 45·4 |

In the cat:—

| | Fæces. | Urine. | Respiration and Perspiration. |
|---|---|---|---|
| Water . . | 1·2 per cent. | 82·9 per cent. | 15·9 per cent. |
| Carbon . . | 1·2 „ | 9·5 „ | 89·4 „ |
| Hydrogen . . | 1·1 „ | 23·2 „ | 75·6 „ |
| Nitrogen . . | 0·2 „ | 99·1 „ | 0·7 „ |
| Oxygen . . | 0·2 „ | 4·1 „ | 95·7 „ |
| Sulphur . . | 50·0 „ | 50·0 „ | — |
| Salts . . . | 92·9 „ | 7·1 „ | — |

From these and other data of a similar kind, it appears that far less water is absorbed from the intestinal canal of herbivorous than from that of carnivorous animals. While in the horse and in the cow only about half of the water is absorbed, in cats and dogs as much as seventeen-twentieths are absorbed: again, in the former animals, only from 15 to 20% of the water that has been absorbed or that has been formed within the system, is removed by the kidneys, while in the latter about 80% passes off to the urine.

The fact that the absorbed carbon is excreted in far larger quantities through the lungs in the herbivora than in the carnivora (the carbon in the urine being to the carbon in the

respiratory products as 1 to 19 in the former, and as 1 to 9·5 in the latter), probably depends solely on the nature of the food, and not upon any special relations of the organism; for while the carbo-hydrates which enter largely into the food of the herbivora are completely resolved into carbonic acid and water, and have yielded little or nothing to the urine, the nitrogenous food of the carnivora is, for the most part, ultimately reduced into urea, which contains a considerable quantity (20%) of unoxidised carbon.

For the same reason we find that much less hydrogen is eliminated through the kidneys in the herbivora than in the carnivora; the ratio of the hydrogen excreted through the urine to that eliminated through the lungs being as 1 to 23 in the herbivora, and as 1 to 3·3 in the carnivora.

The excretion of nitrogen is very different in herbivorous and carnivorous animals; the former often excrete by the lungs and skin 40% of the nitrogen which they had absorbed with the protein-bodies, while the latter rarely excrete more than 1% by these channels. Indeed, Bischoff and Voit's experiments show that all their nitrogen is excreted as urea. The cause of this difference is not altogether clear; but it would almost seem as if the process of oxidation were so energetic in the herbivora that a great part of their urea, instead of being excreted in the form of urea, as in the case of the carnivora, is still further oxidised—a view which is in some measure supported by the ordinary absence in their urine of the earlier and less oxidised product of the decomposition of the albuminates, namely, uric acid. It has been suggested that the greater desquamation of the cuticle and the more rapid growth and falling off of the hair in the herbivora than in the carnivora, may partly account for this difference, as these textures are rich in nitrogen; as far as I know, this view has not, however, been confirmed by any trustworthy experiments or observations.

Our limits will not permit of our entering at any length

into the researches of Bidder and Schmidt, and the more recent investigations of Bischoff and Voit, on the nutrition of the carnivora.

The following table from Bidder and Schmidt is, however, so important as showing the ultimate destiny (if we may use such an expression) of the food, that it must not be omitted. The experiments I., II., III., were made on an adult cat weighing 3200 grammes, while IV. was made on a kitten weighing 1170 grammes. We take the flesh that was consumed (that is to say, its dried residue) as the unit, and calculate the amount of solid matters which pass away in the urine and fæces, the exhaled carbonic acid, and the aqueous vapour; but exclude from our consideration the water that has been taken, and that is separated by the solid and fluid excretions.

I. has reference to the metamorphosis of tissue when the minimum necessary quantity of food was taken, there being free access to water.

II. has reference to the greatest possible quantity of food, with free access to water.

III. has reference to a normal flesh diet (that is to say, one in which the weight of the body remains constant) without water.

IV. has reference to another animal, with flesh and water *ad libitum*.

| | I. | II. | III. | IV. |
|---|---|---|---|---|
| Dried flesh . . | 100·0 | 100·0 | 100·0 | 100·0 |
| Absorbed oxygen . | 167·0 | 166·0 | 167·3 | 166·2 |
| Solid residue of the urine | 31·3 | 30·4 | 30·6 | 31·4 |
| Solid residue of the fæces | 1·7 | 2·5 | 1·7 | 2·0 |
| Exhaled carbonic acid | 182·0 | 181·4 | 182·6 | 181·4 |
| Exhaled aqueous vapour | 137·6 | 76·4 | 152·6 | 128·7 |

From this table we see that the flesh taken as food undergoes in the body a species of analysis, which gives as accurately defined values, as if it underwent in the laboratory a process of fermentation or combustion, and we find that

under all conditions one part of dry flesh is decomposed in the living body, with the co-operation of 1·67 parts of oxygen, into 0·31 of urinary matters, 0·02 of fæcal matters, and 1·82 of carbonic acid.

Since the lean flesh that was used in these experiments contained 19·56% of albuminous and gelatigenous matters, 4·74% of fat, 1% of inorganic matters, and 74·7% of water, while the solid residue of the urine, during such a diet, contains on an average 85·5% of urea and 14·5% of salts (in which are 2·3% of sulphuric acid), and that of the fæces about 63% of biliary residue, the following balance may be struck between the income and the expenditure of a carnivorous animal, if we assume (which is very nearly the case) that for every thousand grammes of its bodily weight, the animal consumes daily fifty grammes of flesh.

| An animal, for every 1000 grammes, *consumes* in 24 hours,— | Water. | Albumen and gelatigenous matters. | Fat. | Salts. |
|---|---|---|---|---|
| 50·000 gr. of flesh . . . . | 37·350 | 9·78 | 2·370 | 0·510 |
| 21·125 „ oxygen | | | | |
| Total 71·125 gr. | | | | |

| An animal, for every 1000 grammes, *excretes* in 24 hours,— | Water. | Carbonic Acid. | Urea. | Salts. | Intestinal excretion. | Bile. |
|---|---|---|---|---|---|---|
| 39·468 gr. of perspiration . . | 16·445 | 23·023 | | | | |
| 30·761 „ urine . . . | 26·839 | | 3·53 | 0·569 | | |
| 0·806 „ fæces . . . | 0·681 | | | 0·041 | 0·039 | 0·135 |
| Total 71·125 gr. | 43·965 | | | 0·610 | | |

The excess of water (=6·615 grammes) in the excreta over the ingesta obviously corresponds to the aqueous vapour formed in respiration, while the increase of salts (0·100 of a gramme) must be referred to the oxidation of the sulphur in the albuminates.

The metamorphosis of flesh in the animal body is very essentially modified by the simultaneous use of non-nitrogenous food, such as fat or sugar.

Lehmann, basing his opinions chiefly on the observations

of Bidder and Schmidt, maintains that under all circumstances the use of fat diminishes the metamorphosis of the nitrogenous constituents of the body; thus, for instance (he observes), during an entire deprivation of food, more urea is excreted than when a purely non-nitrogenous diet is given. We generally find that a carnivorous animal, when fed upon a mixture of flesh and fat, excretes much less urea than we should have calculated the ingested protein-compounds to yield; but occasionally rather more urea is excreted than on a purely animal diet. The amount of urea must not, however, be taken as a perfectly correct measure of the amount of metamorphosis of the nitrogenous constituents, since even in adult and old animals, and of course in growing ones, a certain amount of nitrogenous matter is deposited as additional tissue and retained in the body; and further we must not forget that if an excess of fatty food is given, a certain amount of nitrogenous material is required for the formation of the fat-cells; and that on the other hand, under certain conditions, the fat contributes to the formation of the nitrogenous tissues.*

* Bischoff and Voit have carefully studied the effects of different kinds of food on the metamorphosis of the tissues of the dog. As far as I can understand their conclusions (which occasionally seem somewhat contradictory), regarding the use of fat as food, they are as follows: —

1. The metamorphosis of the nitrogenous parts of the body, and the consumption of flesh for their restoration, are not impeded by the use of fat.

2. Fat directly increases the metamorphosis of the nitrogenous tissues in proportion to its quantity.

3. Nevertheless fat invariably checks the metamorphosis of the nitrogenous tissue by a definite amount which exceeds the increased metamorphosis just noticed. Although this influence of the fat in diminishing the metamorphosis is not in itself great, we find that the quantity of flesh which we give simultaneously with fat, need not be more than $\frac{1}{3}$ or $\frac{1}{4}$ of what we should give without fat, to keep the body at its normal weight.

4. The consumption of the fat in the body may be diminished or entirely avoided by the addition of fat to the food.

5. The apparent paradox that the fat both diminishes the consumption of the nitrogenous tissues and food, and at the same time increases the metamorphosis of the muscular tissue, may be explained in this way, that in all possibility the fat is not at once and directly burned in the blood, but first undergoes

(352.) The metamorphosis of the tissues in fasting animals has been carefully studied by Boussingault, Chossat, Bidder and Schmidt, Bischoff and Voit, and others. Different kinds of animals lose different relative amounts of weight before they necessarily die of inanition, the loss ranging from 31 to 52% of the normal weight.* Carnivorous animals (cats) succumb in about eighteen days, after losing 51·7% of their weight: the average daily loss being 2·87%. Other animals lose during inanition 4·2%, or about $\frac{1}{24}$th of their bodily weight; a number which coincides pretty nearly with the daily amount of nitrogenous food which they require. In Schmidt's experiments on cats, the loss of weight was tolerably steady from the beginning to the end. From the first to the eighth day it corresponded to the quantity of carbon that was expired (0·56% to 0·58% of the weight of the body); subsequently the amount of carbon which was excreted sank less than the bodily weight; but it was only during the last two days that it fell very far below the loss of bodily weight.

Metamorphosis of the tissues during inanition.

The secretion of urine at first diminished in a far more rapid proportion than the bodily weight, but afterwards, till

a metamorphosis in some other part (probably the liver), and occasions a removal of the nitrogenous substances.

6. Sugar and starch act in precisely the same way as fat, but these carbohydrates, notwithstanding that they contain less carbon and hydrogen than fat, have a more powerful effect in checking metamorphosis than that substance; the reason probably being that they (especially sugar) are burned directly in the blood.

7. Liebig's division of foods into plastic and respiratory, is fully confirmed by their investigations. Nitrogenous substances are the only producers of force (Krafterzeuger), that is to say, they alone, by their decomposition in the animal body, give rise to the phenomena of motion; while fat and the carbohydrates, by their decomposition, produce no motor effects, but merely develope heat. If we except a few organisms containing cellulose, all animal structures which possess an independent form are constructed of nitrogenous materials.

* Chossat found that rabbits (5 experiments) died when they had lost 37·4% of their weight; guinea-pigs (5) when they had lost 33·0%; turtle-doves (15) when they had lost 37·9%; domestic pigeons (20) when they had lost 41·6%; hens (2) when they had lost 52·7%, and a crow when it had lost 31·1%; the average of the 48 experiments being 39·7%; or 2-5ths of the original weight.

the sixteenth day, the loss proceeded in each in almost the same proportions; the urine, like the carbonic acid, diminishing considerably during the last two days. The urine was richer than usual in phosphoric and sulphuric acids, but the chlorides disappeared after the first few days. The ratio of the sulphuric to the phosphoric acid remained constant throughout the experiment.

Schmidt has calculated the loss of weight of the muscle and fat, for each individual day, from the amount of the excretions. It follows from these calculations (for which we have not space) that the average loss of muscular substance which the animals experienced in twenty-four hours was 0·611% of their weight at the time, while the corresponding loss of fat was 0·422%, and they yielded 2·16% of carbonic acid, 1·6% of perspired and exhaled aqueous vapour, 0·20% of urea, 0·008% of sulphuric acid, 0·011% of phosphoric acid, 0·029% of inorganic urinary constituents, 0·08% of dry fæces (containing 0·02% of biliary residue), and 2·24% of water separated by the kidneys and rectum.

Both Chossat, and Bidder and Schmidt have attempted to determine the amount of loss of each individual organ during inanition. In one of the cats experimented on by the latter observers it appeared that during the eighteen days' inanition, the blood experienced the greatest loss, namely, 93·7% of its original weight; next in order was the pancreas, which lost 85·4%; the loss of fat was 80·7%, that of the muscles and tendons 66·9%, that of the brain and spinal cord 37·6%, and that of the bones 14·3%; the loss experienced by the kidneys was the least, being only 6·2%. Hence the chief loss of weight in the body is mainly due to the destruction of the muscular tissue, the blood, and the fat.

Effect of the abstraction of water.

(353.) The effect of the entire abstraction of water from the food has been studied by Bidder and Schmidt* on the dog,

* Arch. f. phys. Heilk. vol. xii. pp. 61—73, and vol. xiii. pp 508—21. See

by Falck and Scheffer* on the dog and on the pigeon, and by Kunde on the frog. The following are the principal results at which they have arrived:—The animals took much less food than when they were allowed to drink, and consequently their excretions were considerably diminished. During a twelve days' thirst a dog discharged 60 grammes of urine on the first day, 24 grammes on the seventh day, and only 7 grammes on the twelfth day; the skin peeled off, and the hair (and in birds, the feathers) fell off; the excrements were either viscid or hard. The *excreta* far exceeded the *ingesta*, and hence there was a rapid diminution of the bodily weight. In the absence of water pigeons lost daily 3·7% of their weight, and from the twelfth to the thirteenth day (when they died) 4·6%. On an examination of the organs after death, the greatest loss of weight was found to have been incurred by the muscles, the skin, and the fat, while the brain, eyes, and spleen were hardly affected.

(354.) We have hitherto considered the process of metamorphosis in adult animals. If we investigate the question in growing animals the difficulties of the problem are so much increased that we shall omit this portion of the subject altogether.

The intestinal juices as a measure of the metamorphosis.

We may here introduce a notice of one or two of the most important results at which Bidder and Schmidt have arrived, in reference to the metamorphosis of the tissues. We have seen in the second part of this volume that the following numerical data have been established with a fair amount of certainty, partly from direct observation, but chiefly from experiments on dogs.

An adult man weighing 64 kilogrammes (or 10 stone) secretes in twenty-four hours about 1600 grammes of saliva containing 15 grammes of solid matters, 1600 grammes of

also Scheffer, De animalium, aqua iis adempta, nutritione. Diss. inaug. Marburgh, 1852.

* Zeitsch. f. wiss. Zool. vol. viii. pp. 466—86.

bile with 80 of solid constituents, 16,900 grammes of gastric juice with 91 grammes of solid constituents, 4600 grammes of pancreatic juice containing 113 grammes of solid matters, and 200 grammes of intestinal juice containing 3 grammes of solids. Hence in the course of twenty-four hours digestive fluids to the extent of 24,900 grammes (consisting of about 24,600 grammes of water and 300 grammes of solids) are separated from the blood, poured into the intestine, and for the most part are again absorbed. Now, since the body of a man weighing 64 kilogrammes contains about 44 kilogrammes (or 44,000 grammes) of water and 20 kilogrammes (or 20,000 grammes) of solid constituents, it follows that at least half of the water, but only about $\frac{1}{65}$ of the solids, are daily poured into the intestine.

The daily amount of hydrochloric acid contained in the gastric juice is calculated by Schmidt at 3·392 grammes, which requires the decomposition of 5·436 grammes of salt. If the body contains 10 kilogrammes (or about 22 lbs.) of blood with 0·421% of chloride of sodium, about an eighth part of the whole of this constituent must be decomposed in order to yield its due supply of acid, while 2·881 grammes of free soda are liberated.

The following investigations are of importance, as illustrating the connection between the secretion of bile and the respiratory and urinary products. A dog living on mixed food for every kilogramme's weight oxidizes in twenty-four hours 8·6 grammes of carbon, and during the same period secretes 1 gramme of solid biliary matter, and 0·5 of a gramme of the carbon, contained in the latter, returns from the intestine to the blood; hence it follows that from 5 to 6% of the expired carbon has to go through the stage of bile-formation, or in other words, that proportion of expired carbonic acid takes its origin from the bile. This proportion remains tolerably fixed during a flesh diet, but if a great excess of animal food is given the biliary secretion increases

in a greater proportion than the respiratory products. During the use of highly amylaceous food the oxidation of the biliary constituents into carbonic acid is impeded, and the amount of expired carbon considerably exceeds the quantity passing through the bile. When the mineral constituents of the food are much increased the biliary secretion is relatively more augmented than the respiratory products: but during starvation the former is more diminished than the latter. Scarcely 3% of the nitrogen which is contained in the urinary constituents passes through the bile (as taurine and glycine), while from 54 to 86% of the sulphur takes that course; under no conditions, however, does the whole of the sulphur pass through the stage of bile. In herbivorous animals scarcely two-thirds of the glycine contained in the hippuric acid are derived from the glycocholic acid of the bile.

Bidder and Schmidt further determined the amount of the different elements, of the water, and of the salts contained in a carnivorous animal (a young cat, weighing 1505 grammes).

In 100 parts there were contained 32·039 of solid constituents; and in a kilogramme's weight (1000 grammes) there were contained about 679·61 grammes of water, 148·72 grammes of carbon, 20·19 grammes of hydrogen, 35·45 grammes of nitrogen, 54·78 grammes of oxygen, 2·43 grammes of sulphur, 1·88 grammes of sodium, 1·51 grammes of chlorine, 51·02 grammes of earthy phosphates, including about 0·4 of a gramme of iron, and 4·41 grammes of other salts, including 2·12 grammes of phosphoric acid.

From the above (and other) data, Bidder and Schmidt calculate that a dog fed with flesh gives off 2·25 grammes of water by perspiration and respiration, and 5·97 grammes by the urine and fæces (and therefore on the whole 8·22 parts) for every 100 grammes of water which it contains; while 23·25 grammes are effused into the intestine with the digestive or chylopoietic fluids. Hence the intermediate circulation of

water into the intestine involves nearly a fourth part of the whole of the water in the body, and is nearly three times as abundant as the final excretion from the system in the form of perspiration and respiration. If, on the other hand, we consider the blood, we find that in twenty-four hours about 27·9% of its water is entirely removed from the body, while 79·0% is effused into the intestinal canal. Of every 100 parts of salts in a dog fed with flesh there are in twenty-four hours 5·3 given off to the external world, while 8·5 parts are effused with the digestive fluids over the surface of the intestinal canal; while of 100 parts of blood-salts 21·2 parts are completely excreted in twenty-four hours, and 34·1 parts are conveyed into the intestine. Of every 100 parts of carbon in the body 4·26 parts are daily separated by the respiration and urine, while only 1·31 parts pass into the intestine (of which 0·376 proceeds from the bile); and a similar ratio holds good for the hydrogen. Of every 100 parts of nitrogen in the body 3·89 parts are excreted, and only 1·28 parts pass into the intestine (of which not more than 0·101 proceeds from the bile). Of every 100 parts of sulphur in the body 3·3 parts are daily excreted by the kidneys, while 2·6 parts enter the intestinal juices (1·7 of which is derived from the bile). Of 100 parts of the phosphoric acid of the soluble phosphates of the body, there are daily eliminated 7·27 parts, while 2·9 are effused into the intestine.

The above are merely a few of the striking results to which Bidder and Schmidt's ingenious and original mode of investigation has led them. To those who wish to pursue the subject further, we would especially recommend the careful study of their work, "Die Verdauungssäfte und der Stoffwechsel," and of the chapter headed "Statistische Uebersicht des Stoffwechsels," in the first volume of Funke's Lehrbuch der Physiologie.

On the power which certain sub-

(355.) We shall conclude this fragmentary chapter with a brief notice of the power which certain substances, as for

instance alcohol and tobacco, seem to exert in modifying the ordinary metamorphosis of the tissues.

stances exert in checking the metamorphosis of the tissues.

The physiological effects of alcohol upon the human system have been very carefully examined by Dr. Böcker and more recently by Dr. Hammond. We shall give the conclusions at which Dr. Hammond has arrived from a series of careful experiments upon himself.

He had the three following objects in view in his investigations regarding alcohol.

The physiological action of alcohol.

1. To observe its effects upon a system in which the weight of the body was *maintained at a nearly uniform standard* by a sufficiency of food.

2. To ascertain its influence upon an organism where the body *lost weight* from a deficiency of food.

3. To determine its action upon a system when the body *gained weight* from an excess of food.

(1.) Having ascertained the state of his system in reference to the various excretions, &c., when no alcohol was ingested, and when the food was sufficient to keep the weight constant, Dr. Hammond took four drachms of alcohol diluted with an equal quantity of water at each meal, or twelve drachms daily; and he continued this course for five days. I give the results of the experiment in nearly his own words. After the use of sixty drachms of alcohol in five days, his weight increased from an average of 226·40 lbs., to an average of 226·85 lbs., being ·45 of a lb. of difference. The carbonic acid and vapour of water in the expired air had respectively decreased 1324·5 and 196·5 grains, the fæces 1·2 ounces, and the urine 3·4 ounces daily (its urea being diminished 87·2 grains, its chlorine 37·6 grains, its phosphoric acid 24·5 grains, and its sulphuric acid 13·4 grains). The free acid and the uric acid were apparently not affected.

The general health was somewhat disturbed, there being headache and increased heat of skin; and the mental faculties not being so clear as when no alcohol was taken. There was

indisposition to any kind of exertion; appetite variable; digestion not affected.

The metamorphosis of tissue and fat was evidently considerably retarded, as is shown by the decreased amount of urea, carbonic acid, &c. Dr. Hammond ascribes the diminution in the weight of the fæces mainly to the increased assimilation of food induced by the alcohol.

As alcohol cannot be converted into tissue, the increase in the weight of the body was probably owing to the three following causes: —

1. The retardation of the decay of the tissues.
2. The diminution in the consumption of the fat.
3. The increase in the assimilative powers of the system, by which the food was more completely appropriated and applied to the formation of tissue.

From the results of the foregoing experiments Dr. Hammond concludes, that when the food is sufficient for the requirements of the system alcohol is injurious, by exciting the circulation and tending to induce a plethoric habit of body; its influence in this respect being the same as that of an excessive amount of food. When, therefore, alcohol is taken in addition to a sufficient quantity of food, its effects should be counteracted by the employment of means for the accelerated destruction of the tissues, as for instance, by increased muscular exercise, or by the free use of water (see p. 298); the action of chloride of sodium is also to some extent antagonistic to that of alcohol.

(2.) Dr. Hammond reduced his daily food for five days to such an extent as to induce a daily loss of weight, and a certain amount of exhaustion, and then additionally took the same quantities of alcohol as in his first experiment. Before beginning the alcohol his weight decreased an average of ·28 of a pound daily, falling in five days from 226·73 to 225·34 lbs. Under the use of alcohol for five days this decrease was not only overcome, but there was an actual average daily

increase of ·03 of a pound, the weight rising from 225·34 to a mean of 225·50 lbs.

The expired carbonic acid exhibited an average decrease of 729 grains, the aqueous vapour of 312 grains, the fæces of ·19 of an ounce, and the urine of 1·37 ounces (the urea being diminished 54·5 grains, the chlorine 10·1 grains, the phosphoric acid 8·7 grains, and the sulphuric acid 1·1 grain). The acidity of the urine and the uric acid were slightly increased.

The general condition of his system was never better.

"The good effects," he observes, "of alcohol in limiting the waste of the body when the supply of food is not sufficient to maintain the vigour of the system are here very evident, and stand in marked contrast to its influence when an abundance of food was ingested. The strength was not only sustained, but the body gained weight. In short, the alcohol had taken the place of the bread and meat omitted, and at no apparent disadvantage to the general economy."

(3.) When the body was gaining weight from excess of food he found that the weight was further increased by the use of alcohol, which, as in the previous cases, diminished all the products of excretion. During the five days on which this experiment was continued, the general health was much disordered, there being constant headache, disturbed sleep, hot skin, quick (98), full, and bounding pulse, &c.

From a general review of his three sets of experiments he arrives at the conclusion, "that alcohol increases the weight of the body by retarding the metamorphosis of the old and promoting the formation of new tissues, and limiting the consumption of fat."

The respiratory and urinary excretions, and the fæces were invariably diminished. These effects occurring when the amount of food was below the quantity required to maintain the weight of the body under the mental and physical exer-

cise taken, were productive of no deleterious results to the system; but when the food was sufficient to balance the waste from the excretions, and still more so when an excess of aliment over the demands of the system was ingested, the health was disturbed, and actual disease almost induced.

"The use of alcohol, even in moderation, cannot therefore be either exclusively approved or condemned. The labouring man, who can hardly procure bread and meat enough to preserve the balance between the formation and decay of his tissues, finds here an agent which, within the limits of health, enables him to dispense with a certain quantity of food, and yet keeps up the strength and weight of his body. On the other hand, he who uses alcohol when his food is more than sufficient to supply the waste of tissue, and at the same time does not increase the amount of his physical exercise, or drink an additional quantity of water (by which the decay of tissue would be accelerated), retards the metamorphosis while an increased amount of nutriment is being assimilated, and thus adds to the plethoric condition of the system, which excessive food so generally induces."*

The physiological action of tobacco.

With regard to tobacco Dr. Hammond made two sets of experiments; (1) when a sufficiency of food was taken to keep up the weight and vigour of the body, and (2) when an insufficiency of food was taken. It should be mentioned that he is not in the habit of using tobacco in any form, and that during these experiments he smoked 450 grains daily. He finds:—

1. That tobacco does not materially affect the excretion of carbonic acid through the lungs, but that it lessens the amount of aqueous vapour.

* Moleschott, a well-known German authority on dietetics, some years ago arrived at almost precisely similar conclusions regarding the moderate use of alcohol by ill-fed, hard-working men. The subject is discussed in a very philosophic spirit by Dr. Chambers, in his excellent work on "Digestion and its Derangements."

2. That it diminishes the amount of fæces.

3. That it lessens the quantity of the urine and the amount of its urea and chlorine, but that it increases the amount of free acid, and of the uric, phosphoric, and sulphuric acids.

These results differ in several essential points from those yielded by alcohol. The fact that the amount of carbonic acid was not diminished would indicate that the consumption of the fat of the body is not lessened by the use of tobacco. The general metamorphosis of the tissues would seem to be retarded, seeing that both the urea and the chlorine of the urine are diminished (in the first set of experiments the mean daily diminution of urea and of chlorine was represented by 42·4 and 23·0 grains; while in the second set the corresponding numbers were 62·5 and 15·0 grains): but as the phosphoric and sulphuric acids are increased (in the first set the mean increase being 24·2 and 4·4 grains, and in the second set 30·2 and 8·3 grains), we can only explain the apparent inconsistency in these results by assuming that there is an increased oxidation of the phosphorus and sulphur of the brain and nervous tissue generally, although the metamorphosis of the other nitrogenous tissues is lessened.

Tobacco resembles alcohol in these respects, that when the food is sufficient to preserve the weight of the body it increases that weight, and when the food is not sufficient and the body in consequence loses weight, it restrains that loss: but it differs from alcohol in being unattended with any unpleasant effects upon the circulatory system, though its action on the brain is apparent in increased nervous excitement, followed by a pleasant feeling of ease and contentment.

Physiological action of tea.

Tea and coffee are usually believed to have a somewhat similar effect to that which, as we have shown, is produced by alcohol and tobacco.

Böcker * made a careful series of observations upon himself, for the purpose of testing the effects of tea on the organism.

Three series of experiments were made under varying conditions, but they all coincided in the following particulars:—

1. Tea in ordinary doses has not any effect on the amount of carbonic acid expired, the frequency of the respirations, or of the pulse.

2. When the diet is insufficient, tea very considerably limits the loss of weight thereby entailed.

3. When the diet is sufficient the body is more likely to gain weight when tea is taken than when not.

4. Tea very much diminishes the loss of substance in the shape of urea.

5. Tea very much lessens the quantity of fæces.

6. The loss by perspiration is also limited by tea.

Dr. Edward Smith has recently arrived at certain conclusions which are the very reverse of those of Böcker. He maintains that tea increases the amount of carbonic acid (and here he is likewise opposed to other observers; see p. 477), and that it actually accelerates the waste of the tissues. It is to be trusted that this discrepancy of opinion between two good observers may lead to this important question being further examined and definitely settled.

Of coffee. The action of coffee on the organism has been carefully studied by Dr. Julius Lehmann.† He has investigated the separate actions of the different constituents of the coffee-bean, viz.: caffeine (identical with theeine) and empyreumatic oil, as well as of their mixture. The point that mainly concerns us in reference to the present subject, is (1) that coffee protracts the decomposition of the tissues, and (2) that the protraction is chiefly caused by the empyreumatic oil,

* Archiv des Vereins f. gemeinschaftlichen Arbeiten 1853; or Chambers op. cit. p. 246.

† Ann. d. Ch. u. Pharm. vol. lxxvii. p. 205.

and that the caffeine only causes it when it is taken in larger quantities than usual.

For further information on this subject the reader may consult Dr. Chambers's remarks on "Arresters of Metamorphosis," in the work already referred to.

# EXPLANATION OF THE PLATES.

## PLATE I.

*Fig.* 1. Oxalate of lime in the form in which it most commonly appears in ordinary deposits.

*Fig.* 2. (*a.*) Oxalate of lime, (*b.*) Carbonate of lime, deposited from the urine of the horse. This form occasionally presents itself in alkaline human urine. (*c.*) Urate of soda, from a urinary sediment. We thus see that dumb-bell crystals do not of necessity imply the presence of oxalate of lime. See also *Plate III. fig.* 4, where uric acid is represented in the same form.

*Fig.* 3. Margaric acid, deposited from an alcoholic solution.

*Fig.* 4. Stearic acid, deposited from an alcoholic solution.

*Fig.* 5. (Misprinted *fig.* 3 in p. 16.) Sebacic acid, deposited from a hot solution.

*Fig.* 6. Lactate of lime, obtained from pure lactic acid and carbonate of lime, and crystallised from a hot aqueous solution.

*Fig.* 7. Cholic acid, obtained by treating glycocholate or taurocholate of soda with caustic potash or baryta.

*Fig.* 8. Glycine, obtained by the digestion of gelatin with caustic potash, and crystallised from water.

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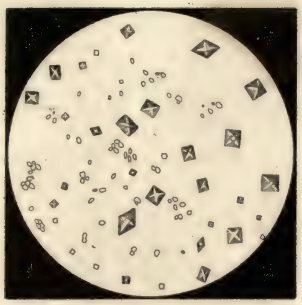

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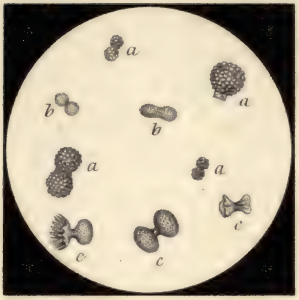


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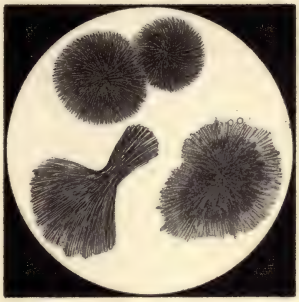

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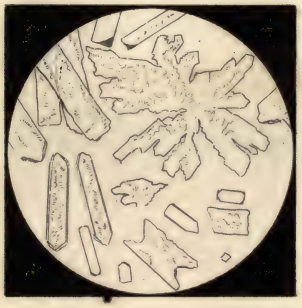

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## PLATE II.

*Fig.* 1. Leucine, obtained by the digestion of albumen in concentrated sulphuric acid.

*Fig.* 2. Creatine, obtained from beef by Liebig's method, and crystallised from hot water.

*Fig.* 3. Creatinine, obtained from creatine by digestion with hydrochloric acid, from which it is separated by hydrated peroxide of lead, and crystallised from a hot aqueous solution.

*Fig.* 4. Urea from human urine; crystallised slowly from an aqueous solution.

*Fig.* 5. Nitrate of urea.

*Fig.* 6. Allantoine from calves' urine, recrystallised from hot alcohol.

*Fig.* 7. Cystine, obtained from a calculus, and crystallised from an ammoniacal solution.

*Fig.* 8. Taurine from ox-bile, crystallised from a boiling aqueous solution.

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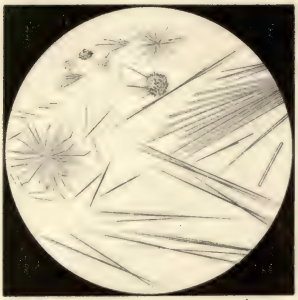

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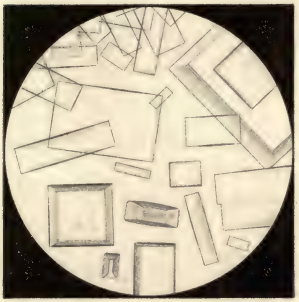

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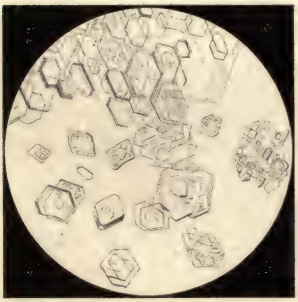

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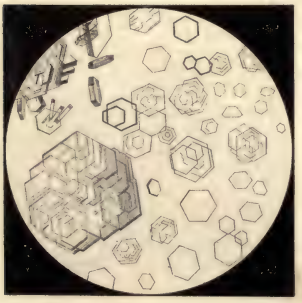

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## PLATE III.

*Fig.* 1. Hippuric acid, crystallised from water.

*Fig.* 2. Glycocholic acid obtained by treating glycocholate of soda with sulphuric acid, and crystallised from a spirituous solution by the addition of ether.

*Fig.* 3. Glycocholate of soda, from ox-bile, crystallised from an alcoholic solution by the addition of ether.

*Fig.* 4. Uric acid in various forms.

*Fig.* 5. Urate of soda, obtained artificially by the digestion of pure uric acid with phosphate of soda. See also *Plate I. fig.* 2.

*Fig.* 6. Urate of ammonia obtained by treating the preceding salt with hydrochlorate of ammonia.

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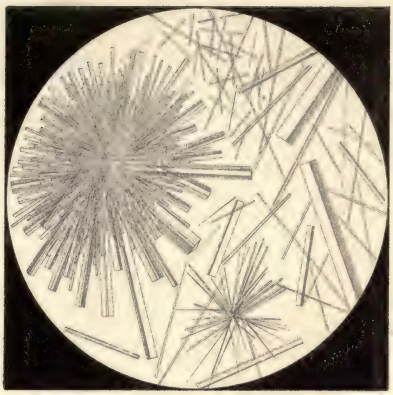

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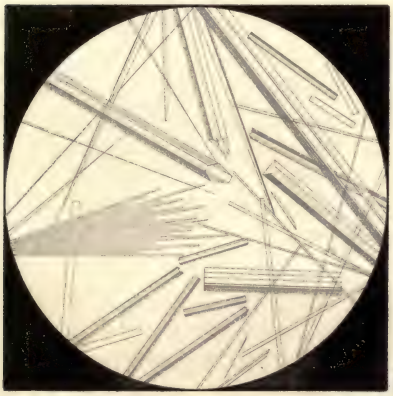

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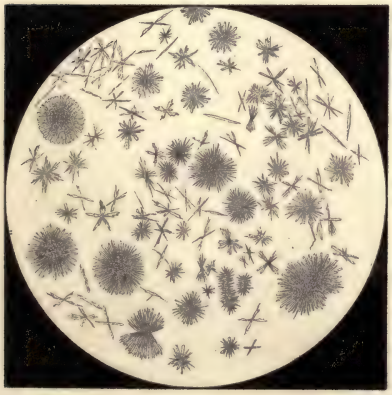

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## PLATE IV.

*Fig.* 1. Stearin from mutton suet, crystallised from an ethereal solution.

*Fig.* 2. Margarin, deposited from an alcoholic solution.

*Fig.* 3. Cholesterin, from the contents of a partly obliterated echinococcus-sac in the liver. In addition to the tablets of cholesterin, the plate exhibits tufts of crystals of margaric acid, roundish dark-coloured pigment-granules, and small crystals of hæmatoidin. The whole extent is strewed over with fat-globules and minute yellow amorphous aggregations of bile and biliary products.

*Fig.* 4. Hæmatocrystallin. (*a.*) Blood-crystals from normal human venous blood. (*b.*) Blood-crystals from the blood in the heart of a kitten. (*c.*) Blood-crystals from the jugular vein of a guinea-pig. (*d.*) Blood-crystals from the jugular vein of a squirrel. I have selected these different figures with the view of showing the various forms in which this substance crystallises.

*Fig.* 5. A urinary sediment consisting of triple phosphates (phosphate of ammonia and magnesia), and of urate of ammonia, thrown down by a specimen of urine that had undergone alkaline fermentation, and which had been passed by a man with paralysis of the lower extremities consequent on disease of the spinal cord.

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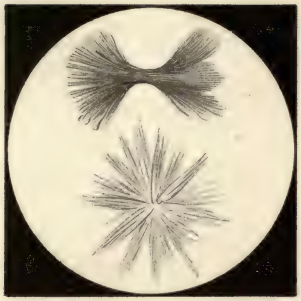

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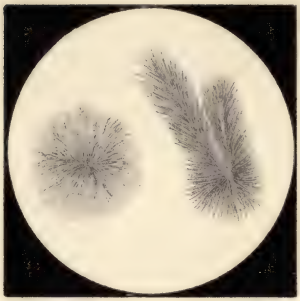

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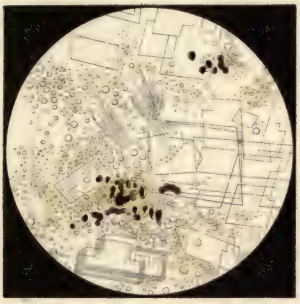

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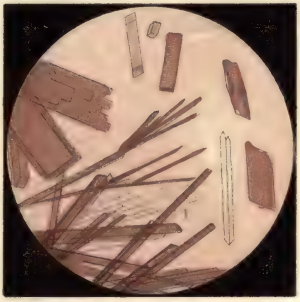

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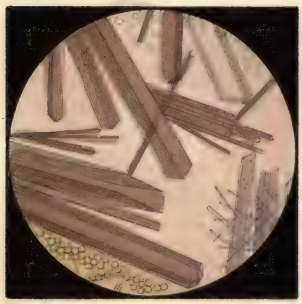

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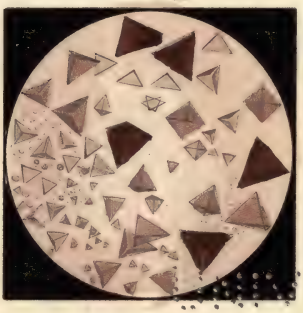

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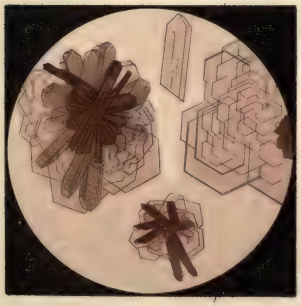

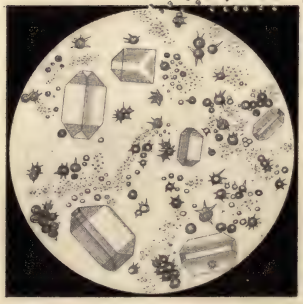

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## PLATE V.

*Fig.* 1. A urinary sediment consisting of the *Torula* or *Mykoderma Cerevisiæ* and Confervæ, formed in diabetic urine after exposure for a week to the air.

*Fig.* 2. The epithelium occurring in the "rice-water" discharges in cholera. Crystals of triple phosphates are scattered amongst the epithelial scales. Certain cell-like structures are also apparent.

*Fig.* 3 and *fig.* 4. I had originally intended to have given two figures of the red corpuscles of the blood, one showing them in the separate, and the other in the nummular form. The figure I have selected shows, however, all that is required. A few colourless corpuscles are interspersed.

*Fig.* 5. The white or colourless corpuscles from a specimen of leucæmic blood taken from a man with an enormously enlarged spleen. They are here as numerous as the red corpuscles.

*Fig.* 6. I had intended to have given a separate figure of the chyle-corpuscles, but they so closely resemble the colourless corpuscles exhibited in the preceding figure, that, on further consideration, I deemed it unnecessary to do so.

*Fig.* 7. (*a.*) Milk from a healthy woman a week after delivery.

*Fig.* 7. (*b.*) Colostrum from a healthy woman twelve hours after delivery.

*Fig.* 8. (*a.*) Healthy human pus. In the lower half of the figure the pus-corpuscles are shown in their normal state; in the upper half they have been acted on by acetic acid.

*Fig.* 8. (*b.*) Pus that has undergone acid fermentation; the result of two months' exposure to the air.

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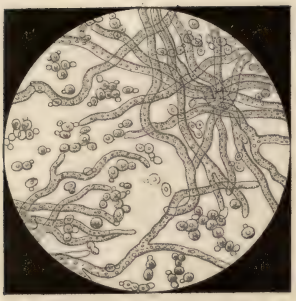

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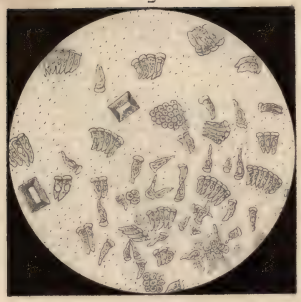

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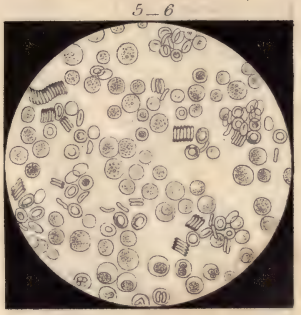

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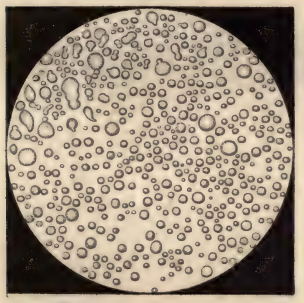

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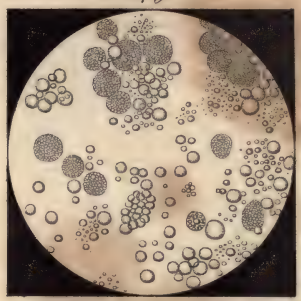

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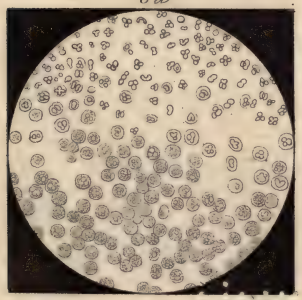

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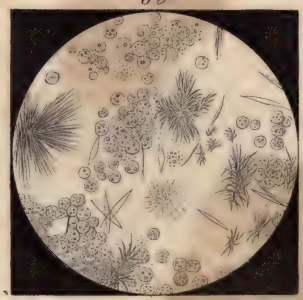

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